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(54) Title: HETEROARYL-PHENYL SUBSTITUTED FACTOR XA INHIBITORS

(57) Abstract: The present application describes heteroaryl-phenyl substituted compounds and derivatives thereof, or pharmaceutically acceptable salt or prodrug forms thereof, which are useful as inhibitors of factor Xa.

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## TITLE

Heteroaryl-Phenyl Substituted Factor Xa Inhibitors

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## FIELD OF THE INVENTION

This invention relates generally to heteroaryl-phenyl substituted compounds and derivatives thereof, which are inhibitors of trypsin-like serine protease enzymes, especially factor Xa, pharmaceutical compositions containing the same, and methods of using the same as anticoagulant agents for treatment and prevention of thromboembolic disorders.

## BACKGROUND OF THE INVENTION

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Activated factor Xa, whose major practical role is the generation of thrombin by the limited proteolysis of prothrombin, holds a central position that links the intrinsic and extrinsic activation mechanisms in the final common pathway of blood coagulation. The generation of thrombin, the final serine protease in the pathway to generate a fibrin clot, from its precursor is amplified by formation of prothrombinase complex (factor Xa, factor V,  $\text{Ca}^{2+}$  and phospholipid). Since it is calculated that one molecule of factor Xa can generate 138 molecules of thrombin (Elodi, S., Varadi, K.: Optimization of conditions for the catalytic effect of the factor IXa-factor VIII Complex: Probable role of the complex in the amplification of blood coagulation. *Thromb. Res.* **1979**, 15, 617-629), inhibition of factor Xa may be more efficient than inactivation of thrombin in interrupting the blood coagulation system.

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Therefore, efficacious and specific inhibitors of factor Xa are needed as potentially valuable therapeutic agents for the treatment of thromboembolic disorders. It is thus desirable to discover new factor Xa inhibitors.

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## SUMMARY OF THE INVENTION

Accordingly, one object of the present invention is to provide novel heteroaryl-phenyl substituted compounds and derivatives thereof that are useful as factor Xa inhibitors or pharmaceutically acceptable salts or prodrugs thereof.

It is another object of the present invention to provide pharmaceutical compositions comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of at least one of the compounds of the present invention or a pharmaceutically acceptable salt or prodrug form thereof.

It is another object of the present invention to provide a method for treating thromboembolic disorders comprising administering to a host in need of such treatment a therapeutically effective amount of at least one of the compounds of the present invention or a pharmaceutically acceptable salt or prodrug form thereof.

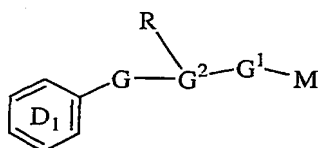
It is another object of the present invention to provide novel heteroaryl-phenyl substituted compounds for use in therapy.

It is another object of the present invention to provide the use of novel heteroaryl-phenyl substituted compounds for the manufacture of a medicament for the treatment of a thromboembolic disorder.

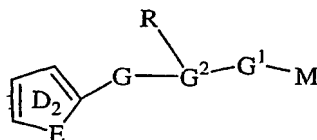
These and other objects, which will become apparent during the following detailed description, have been achieved by the inventors' discovery that the presently claimed heteroaryl-phenyl substituted compounds and derivatives thereof, or pharmaceutically acceptable salt or prodrug forms thereof, are effective factor Xa inhibitors.

## DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

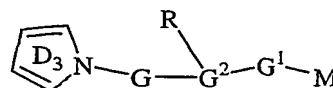
[1] Thus, in a first embodiment, the present invention provides a novel compound of formula Ia, Ib, or Ic:



Ia



Ib



Ic

or a stereoisomer or pharmaceutically acceptable salt  
 5 thereof, wherein;

ring D<sub>1</sub> is selected from pyridine, pyrazine, pyridazine, and  
 pyrimidine and is substituted with 1 R<sup>a</sup> and 0-1 R<sup>b</sup>;

10 ring D<sub>2</sub> is a 5-membered heteroaromatic ring system  
 comprising E, carbon atoms, and 0-3 N atoms, wherein E  
 is selected from O, S, and N-R<sup>c</sup> and ring D<sub>2</sub> is  
 substituted with 1 R<sup>a</sup> and 0-1 R<sup>b</sup>;

15 ring D<sub>3</sub> is a 5-membered heteroaromatic ring system  
 comprising carbon atoms and from 0-3 additional N atoms  
 and ring D<sub>3</sub> is substituted with 1 R<sup>a</sup> and 0-1 R<sup>b</sup>;

R is selected from H, C<sub>1-4</sub> alkyl, F, Cl, Br, I, OH, OCH<sub>3</sub>,  
 20 OCH<sub>2</sub>CH<sub>3</sub>, OCH(CH<sub>3</sub>)<sub>2</sub>, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CN, C(=NR<sup>8</sup>)NR<sup>7</sup>R<sup>9</sup>,  
 NHC(=NR<sup>8</sup>)NR<sup>7</sup>R<sup>9</sup>, NR<sup>8</sup>CH(=NR<sup>7</sup>), NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub>  
 alkyl)<sub>2</sub>, C(=NH)NH<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>N(C<sub>1-3</sub>  
 alkyl)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>CH<sub>2</sub>N(C<sub>1-3</sub>  
 alkyl)<sub>2</sub>, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>NR<sup>7</sup>R<sup>8</sup>, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>C(O)NR<sup>7</sup>R<sup>8</sup>, and OCF<sub>3</sub>;

25

R<sup>a</sup> is selected from H, C<sub>1-4</sub> alkyl, F, Cl, Br, I, OH, OCH<sub>3</sub>,  
 OCH<sub>2</sub>CH<sub>3</sub>, OCH(CH<sub>3</sub>)<sub>2</sub>, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CN, C(=NR<sup>8</sup>)NR<sup>7</sup>R<sup>9</sup>,  
 NHC(=NR<sup>8</sup>)NR<sup>7</sup>R<sup>9</sup>, NR<sup>8</sup>CH(=NR<sup>7</sup>), NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub>  
 alkyl)<sub>2</sub>, C(=NH)NH<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>N(C<sub>1-3</sub>  
 30 alkyl)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>CH<sub>2</sub>N(C<sub>1-3</sub>  
 alkyl)<sub>2</sub>, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>NR<sup>7</sup>R<sup>8</sup>, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>C(O)NR<sup>7</sup>R<sup>8</sup>, and OCF<sub>3</sub>;

$R^b$  is selected from H,  $C_{1-4}$  alkyl, F, Cl, Br, I, OH,  $OCH_3$ ,  
 $OCH_2CH_3$ ,  $OCH(CH_3)_2$ ,  $OCH_2CH_2CH_3$ , CN,  $C(=NR^8)NR^7R^9$ ,  
 $NHC(=NR^8)NR^7R^9$ ,  $NR^8CH(=NR^7)$ ,  $NH_2$ ,  $NH(C_{1-3} \text{ alkyl})$ ,  $N(C_{1-3}$   
 5  $\text{alkyl})_2$ ,  $C(=NH)NH_2$ ,  $CH_2NH_2$ ,  $CH_2NH(C_{1-3} \text{ alkyl})$ ,  $CH_2N(C_{1-3}$   
 $\text{alkyl})_2$ ,  $CH_2CH_2NH_2$ ,  $CH_2CH_2NH(C_{1-3} \text{ alkyl})$ ,  $CH_2CH_2N(C_{1-3}$   
 $\text{alkyl})_2$ ,  $(CR^8R^9)_tNR^7R^8$ ,  $(CR^8R^9)_tC(O)NR^7R^8$ , and  $OCF_3$ ;

$R^c$  is selected from H,  $C_{1-4}$  alkyl,  $OCH_3$ ,  $OCH_2CH_3$ ,  $OCH(CH_3)_2$ ,  
 10  $OCH_2CH_2CH_3$ ,  $NH_2$ ,  $NH(C_{1-3} \text{ alkyl})$ ,  $N(C_{1-3} \text{ alkyl})_2$ ,  
 $C(=NH)NH_2$ ,  $CH_2NH_2$ ,  $CH_2NH(C_{1-3} \text{ alkyl})$ ,  $CH_2N(C_{1-3} \text{ alkyl})_2$ ,  
 $CH_2CH_2NH_2$ ,  $CH_2CH_2NH(C_{1-3} \text{ alkyl})$ ,  $CH_2CH_2N(C_{1-3} \text{ alkyl})_2$ ,  
 $(CR^8R^9)_tNR^7R^8$ ,  $(CR^8R^9)_tC(O)NR^7R^8$ , and  $OCF_3$ ;

15  $G$  is absent or is selected from  $CH_2$ ,  $C(O)$ ,  $O$ ,  $NR^3$ ,  $S(O)_p$ ,  
 $CH_2CH_2$ ,  $C(O)CH_2$ ,  $CH_2C(O)$ ,  $OCH_2$ ,  $CH_2O$ ,  $NR^3CH_2$ ,  $CH_2NR^3$ ,  
 $S(O)_pCH_2$ ,  $CH_2S(O)_p$ ,  $CH_2CH_2CH_2$ ,  $C(O)CH_2CH_2$ ,  $CH_2C(O)CH_2$ ,  
 $CH_2CH_2C(O)$ ,  $OCH_2CH_2$ ,  $CH_2OCH_2$ ,  $CH_2CH_2O$ ,  $NR^3CH_2CH_2$ ,  $CH_2NR^3CH_2$ ,  
 $CH_2CH_2NR^3$ ,  $S(O)_pCH_2CH_2$ ,  $CH_2S(O)_pCH_2$ , and  $CH_2CH_2S(O)_p$ ;

20  $G_1$  is absent or is selected from  $(CR^3R^{3a})_{1-5}$ ,  
 $(CR^3R^{3a})_{0-2}CR^3=CR^3(CR^3R^{3a})_{0-2}$ ,  $(CR^3R^{3a})_{0-2}C\equiv C(CR^3R^{3a})_{0-2}$ ,  
 $(CR^3R^{3a})_uC(O)(CR^3R^{3a})_w$ ,  $(CR^3R^{3a})_uC(O)O(CR^3R^{3a})_w$ ,  
 $(CR^3R^{3a})_uOC(O)(CR^3R^{3a})_w$ ,  $(CR^3R^{3a})_uO(CR^3R^{3a})_w$ ,  
 25  $(CR^3R^{3a})_uNR^3(CR^3R^{3a})_w$ ,  $(CR^3R^{3a})_uC(O)NR^3(CR^3R^{3a})_w$ ,  
 $(CR^3R^{3a})_uNR^3C(O)(CR^3R^{3a})_w$ ,  $(CR^3R^{3a})_uOC(O)NR^3(CR^3R^{3a})_w$ ,  
 $(CR^3R^{3a})_uNR^3C(O)O(CR^3R^{3a})_w$ ,  $(CR^3R^{3a})_uNR^3C(O)NR^3(CR^3R^{3a})_w$ ,  
 $(CR^3R^{3a})_uNR^3C(S)NR^3(CR^3R^{3a})_w$ ,  $(CR^3R^{3a})_uS(CR^3R^{3a})_w$ ,  
 $(CR^3R^{3a})_uS(O)(CR^3R^{3a})_w$ ,  $(CR^3R^{3a})_uS(O)_2(CR^3R^{3a})_w$ ,  
 30  $(CR^3R^{3a})_uS(O)NR^3(CR^3R^{3a})_w$ ,  $(CR^3R^{3a})_uNR^3S(O)_2(CR^3R^{3a})_w$ ,  
 $(CR^3R^{3a})_uS(O)_2NR^3(CR^3R^{3a})_w$ , and  $(CR^3R^{3a})_uNR^3S(O)_2NR^3(CR^3R^{3a})_w$ ,  
 wherein  $u + w$  total 0, 1, 2, 3, or 4, provided that  $G_1$   
 does not form a N-N, N-O, N-S,  $NCH_2N$ ,  $NCH_2O$ , or  $NCH_2S$   
 bond with either group to which it is attached;

G<sup>2</sup> is phenyl, naphthyl, or a 5-10 membered heteroaryl consisting of carbon atoms and from 1-3 heteroatoms selected from N, O, and S;

5

M is isoxazoline, pyrazoline, isothiazoline, triazoline, tetrazoline, phenyl, or a 5-6 membered aromatic heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from O, N, and S, and is substituted with -Z-A-B;

10

M is also substituted with 0-2 R<sup>1a</sup>;

Z is selected from a bond,  $-(CR^2R^{2a})_{1-4}-$ ,  $(CR^2R^{2a})_qO(CR^2R^{2a})_{q^1}$ ,  
 15  $(CR^2R^{2a})_qNR^3(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qC(O)(CR^2R^{2a})_{q^1}$ ,  
 $(CR^2R^{2a})_qC(O)O(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qOC(O)(CR^2R^{2a})_{q^1}$ ,  
 $(CR^2R^{2a})_qC(O)NR^3(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qNR^3C(O)(CR^2R^{2a})_{q^1}$ ,  
 $(CR^2R^{2a})_qOC(O)O(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qOC(O)NR^3(CR^2R^{2a})_{q^1}$ ,  
 $(CR^2R^{2a})_qNR^3C(O)O(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qNR^3C(O)NR^3(CR^2R^{2a})_{q^1}$ ,  
 20  $(CR^2R^{2a})_qS(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qS(O)(CR^2R^{2a})_{q^1}$ ,  
 $(CR^2R^{2a})_qS(O)_2(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qSO_2NR^3(CR^2R^{2a})_{q^1}$ ,  
 $(CR^2R^{2a})_qNR^3SO_2(CR^2R^{2a})_{q^1}$ , and  $(CR^2R^{2a})_qNR^3SO_2NR^3(CR^2R^{2a})_{q^1}$ ,  
 wherein q + q<sup>1</sup> total 0, 1, or 2, provided that Z does not form a N-N, N-O, N-S, NCH<sub>2</sub>N, NCH<sub>2</sub>O, or NCH<sub>2</sub>S bond  
 25 with either group to which it is attached;

R<sup>1a</sup> is selected from H,  $-(CH_2)_r-R^{1b}$ ,  $-CH=CH-R^{1b}$ ,  $NCH_2R^{1c}$ ,  
 $OCH_2R^{1c}$ ,  $SCH_2R^{1c}$ ,  $NH(CH_2)_2(CH_2)_tR^{1b}$ ,  $O(CH_2)_2(CH_2)_tR^{1b}$ ,  
 $S(CH_2)_2(CH_2)_tR^{1b}$ ,  $S(O)_p(CH_2)_rR^{1d}$ ,  $O(CH_2)_rR^{1d}$ ,  $NR^3(CH_2)_rR^{1d}$ ,  
 30  $OC(O)NR^3(CH_2)_rR^{1d}$ ,  $NR^3C(O)NR^3(CH_2)_rR^{1d}$ ,  $NR^3C(O)O(CH_2)_rR^{1d}$ ,  
 and  $NR^3C(O)(CH_2)_rR^{1d}$ , provided that R<sup>1a</sup> forms other than an N-halo, N-N, N-S, N-O, or N-CN bond;

alternatively, when two  $R^{1a'}$ 's are attached to adjacent atoms, together with the atoms to which they are attached they form a 5-7 membered ring consisting of: carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, this ring being substituted with 0-2  $R^{4b}$  and comprising: 0-3 double bonds;

$R^{1b}$  is selected from H, C<sub>1-3</sub> alkyl, F, Cl, Br, I, -CN, -CHO, (CF<sub>2</sub>)<sub>r</sub>CF<sub>3</sub>, (CH<sub>2</sub>)<sub>r</sub>OR<sup>2</sup>, NR<sup>2</sup>R<sup>2a</sup>, C(O)R<sup>2c</sup>, OC(O)R<sup>2</sup>, (CF<sub>2</sub>)<sub>r</sub>CO<sub>2</sub>R<sup>2a</sup>, S(O)<sub>p</sub>R<sup>2b</sup>, NR<sup>2</sup>(CH<sub>2</sub>)<sub>r</sub>OR<sup>2</sup>, C(=NR<sup>2c</sup>)NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>C(O)R<sup>2b</sup>, NR<sup>2</sup>C(O)NHR<sup>2b</sup>, NR<sup>2</sup>C(O)<sub>2</sub>R<sup>2a</sup>, OC(O)NR<sup>2a</sup>R<sup>2b</sup>, C(O)NR<sup>2</sup>R<sup>2a</sup>, C(O)NR<sup>2</sup>(CH<sub>2</sub>)<sub>r</sub>OR<sup>2</sup>, SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>SO<sub>2</sub>R<sup>2b</sup>, C<sub>3-6</sub> carbocycle substituted with 0-2  $R^{4a}$ , and 5-10 membered heterocycle consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub> substituted with 0-2  $R^{4a}$ , provided that  $R^{1b}$  forms other than an N-halo, N-N, N-S, N-O, or N-CN bond;

$R^{1c}$  is selected from H, CH(CH<sub>2</sub>OR<sup>2</sup>)<sub>2</sub>, C(O)R<sup>2c</sup>, C(O)NR<sup>2</sup>R<sup>2a</sup>, S(O)R<sup>2b</sup>, S(O)<sub>2</sub>R<sup>2b</sup>, and SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>;

$R^{1d}$  is selected from C<sub>3-13</sub> carbocycle substituted with 0-2  $R^{4a}$ , and 5-13 membered heterocycle consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub> substituted with 0-2  $R^{4a}$ , provided that  $R^{1d}$  forms other than an N-N, N-S, or N-O bond;

$R^2$ , at each occurrence, is selected from H, CF<sub>3</sub>, C<sub>1-6</sub> alkyl, benzyl, C<sub>3-6</sub> carbocyclic residue substituted with 0-2  $R^{4b}$ , and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the

group consisting of N, O, and S substituted with 0-2 R<sup>4b</sup>;

5 R<sup>2a</sup>, at each occurrence, is selected from H, CF<sub>3</sub>, C<sub>1-6</sub> alkyl, benzyl, phenethyl, C<sub>3-6</sub> carbocyclic residue substituted with 0-2 R<sup>4b</sup>, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R<sup>4b</sup>;

10 R<sup>2b</sup>, at each occurrence, is selected from CF<sub>3</sub>, C<sub>1-4</sub> alkoxy, C<sub>1-6</sub> alkyl, benzyl, C<sub>3-6</sub> carbocyclic residue substituted with 0-2 R<sup>4b</sup>, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R<sup>4b</sup>;

15 R<sup>2c</sup>, at each occurrence, is selected from CF<sub>3</sub>, OH, C<sub>1-4</sub> alkoxy, C<sub>1-6</sub> alkyl, benzyl, C<sub>3-6</sub> carbocyclic residue substituted with 0-2 R<sup>4b</sup>, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R<sup>4b</sup>;

20 alternatively, R<sup>2</sup> and R<sup>2a</sup>, together with the atom to which they are attached, combine to form a 5 or 6 membered saturated, partially saturated or unsaturated ring substituted with 0-2 R<sup>4b</sup> and comprising carbon atoms and from 0-1 additional heteroatoms selected from the group consisting of N, O, and S;

25 R<sup>3</sup>, at each occurrence, is selected from H, C<sub>1-4</sub> alkyl, and phenyl;



R<sup>3a</sup>, at each occurrence, is selected from H, C<sub>1-4</sub> alkyl, and phenyl;

R<sup>3b</sup>, at each occurrence, is selected from H, C<sub>1-4</sub> alkyl, and phenyl;

R<sup>3c</sup>, at each occurrence, is selected from C<sub>1-4</sub> alkyl, and phenyl;

R<sup>3d</sup>, at each occurrence, is selected from H, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkyl-phenyl, and C(=O)R<sup>3c</sup>;

A is selected from:

C<sub>3-10</sub> carbocyclic residue substituted with 0-2 R<sup>4</sup>, and 5-12 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R<sup>4</sup>;

B is selected from: H, Y, and X-Y, provided that Z and B are attached to different atoms on A;

X is selected from -(CR<sup>2</sup>R<sup>2a</sup>)<sub>1-4</sub>-, -CR<sup>2</sup>(CR<sup>2</sup>R<sup>2b</sup>)(CH<sub>2</sub>)<sub>t</sub>-, -C(O)-, -C(=NR<sup>1c</sup>)-, -CR<sup>2</sup>(NR<sup>1c</sup>R<sup>2</sup>)-, -CR<sup>2</sup>(OR<sup>2</sup>)-, -CR<sup>2</sup>(SR<sup>2</sup>)-, -C(O)CR<sup>2</sup>R<sup>2a</sup>-, -CR<sup>2</sup>R<sup>2a</sup>C(O)-, -S-, -S(O)-, -S(O)<sub>2</sub>-, -SCR<sup>2</sup>R<sup>2a</sup>-, -S(O)CR<sup>2</sup>R<sup>2a</sup>-, -S(O)<sub>2</sub>CR<sup>2</sup>R<sup>2a</sup>-, -CR<sup>2</sup>R<sup>2a</sup>S-, -CR<sup>2</sup>R<sup>2a</sup>S(O)-, -CR<sup>2</sup>R<sup>2a</sup>S(O)<sub>2</sub>-, -S(O)<sub>2</sub>NR<sup>2</sup>-, -NR<sup>2</sup>S(O)<sub>2</sub>-, -NR<sup>2</sup>S(O)<sub>2</sub>CR<sup>2</sup>R<sup>2a</sup>-, -CR<sup>2</sup>R<sup>2a</sup>S(O)<sub>2</sub>NR<sup>2</sup>-, -NR<sup>2</sup>S(O)<sub>2</sub>NR<sup>2</sup>-, -C(O)NR<sup>2</sup>-, -NR<sup>2</sup>C(O)-, -C(O)NR<sup>2</sup>CR<sup>2</sup>R<sup>2a</sup>-, -NR<sup>2</sup>C(O)CR<sup>2</sup>R<sup>2a</sup>-, -CR<sup>2</sup>R<sup>2a</sup>C(O)NR<sup>2</sup>-, -CR<sup>2</sup>R<sup>2a</sup>NR<sup>2</sup>C(O)-, -NR<sup>2</sup>C(O)O-, -OC(O)NR<sup>2</sup>-, -NR<sup>2</sup>C(O)NR<sup>2</sup>-, -NR<sup>2</sup>-, -NR<sup>2</sup>CR<sup>2</sup>R<sup>2a</sup>-, -CR<sup>2</sup>R<sup>2a</sup>NR<sup>2</sup>-, O, -CR<sup>2</sup>R<sup>2a</sup>O-, and -OCR<sup>2</sup>R<sup>2a</sup>-;

Y is selected from:

C<sub>3-10</sub> carbocyclic residue substituted with 0-2 R<sup>4a</sup>, and  
 5-12 membered heterocyclic system comprising carbon  
 atoms and from 1-4 heteroatoms selected from the group  
 consisting of N, O, and S substituted with 0-2 R<sup>4a</sup>;

5 R<sup>4</sup>, at each occurrence, is selected from H, =O, (CH<sub>2</sub>)<sub>r</sub>OR<sup>2</sup>,  
 (CH<sub>2</sub>)<sub>r</sub>F, (CH<sub>2</sub>)<sub>r</sub>Cl, (CH<sub>2</sub>)<sub>r</sub>Br, (CH<sub>2</sub>)<sub>r</sub>I, C<sub>1-4</sub> alkyl,  
 (CH<sub>2</sub>)<sub>r</sub>CN, (CH<sub>2</sub>)<sub>r</sub>NO<sub>2</sub>, (CH<sub>2</sub>)<sub>r</sub>NR<sup>2</sup>R<sup>2a</sup>, C(O)R<sup>2c</sup>, NR<sup>2</sup>C(O)R<sup>2b</sup>,  
 C(O)NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>C(O)NR<sup>2</sup>R<sup>2a</sup>, C(=NR<sup>2</sup>)NR<sup>2</sup>R<sup>2a</sup>,  
 10 C(=NS(O)<sub>2</sub>R<sup>5</sup>)NR<sup>2</sup>R<sup>2a</sup>, NHC(=NR<sup>2</sup>)NR<sup>2</sup>R<sup>2a</sup>, C(O)NHC(=NR<sup>2</sup>)NR<sup>2</sup>R<sup>2a</sup>,  
 SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>SO<sub>2</sub>-C<sub>1-4</sub> alkyl, NR<sup>2</sup>SO<sub>2</sub>R<sup>5</sup>,  
 S(O)<sub>p</sub>R<sup>5</sup>, (CF<sub>2</sub>)<sub>r</sub>CF<sub>3</sub>, (CH<sub>2</sub>)<sub>r</sub>-CF<sub>3</sub>, NCH<sub>2</sub>R<sup>1c</sup>, OCH<sub>2</sub>R<sup>1c</sup>, SCH<sub>2</sub>R<sup>1c</sup>,  
 N(CH<sub>2</sub>)<sub>2</sub>(CH<sub>2</sub>)<sub>t</sub>R<sup>1b</sup>, O(CH<sub>2</sub>)<sub>2</sub>(CH<sub>2</sub>)<sub>t</sub>R<sup>1b</sup>, S(CH<sub>2</sub>)<sub>2</sub>(CH<sub>2</sub>)<sub>t</sub>R<sup>1b</sup>, 5-6  
 membered carbocycle substituted with 0-1 R<sup>5</sup>, and 5-6  
 15 membered heterocycle consisting of: carbon atoms and  
 1-4 heteroatoms selected from the group consisting of  
 N, O, and S(O)<sub>p</sub> substituted with 0-1 R<sup>5</sup>;

R<sup>4a</sup>, at each occurrence, is selected from H, =O, (CH<sub>2</sub>)<sub>r</sub>OR<sup>2</sup>,  
 20 (CF<sub>2</sub>)<sub>r</sub>CF<sub>3</sub>, (CH<sub>2</sub>)<sub>r</sub>-CF<sub>3</sub>, (CH<sub>2</sub>)<sub>r</sub>-F, (CH<sub>2</sub>)<sub>r</sub>-Br, (CH<sub>2</sub>)<sub>r</sub>-Cl,  
 C<sub>1-4</sub> alkyl, (CH<sub>2</sub>)<sub>r</sub>CN, (CH<sub>2</sub>)<sub>r</sub>NO<sub>2</sub>, (CH<sub>2</sub>)<sub>r</sub>NR<sup>2</sup>R<sup>2a</sup>,  
 (CH<sub>2</sub>)<sub>r</sub>C(O)R<sup>2c</sup>, NR<sup>2</sup>C(O)R<sup>2b</sup>, C(O)NR<sup>2</sup>R<sup>2a</sup>, (CH<sub>2</sub>)<sub>r</sub>N=CHOR<sup>3</sup>,  
 C(O)NH(CH<sub>2</sub>)<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>C(O)NR<sup>2</sup>R<sup>2a</sup>, C(=NR<sup>2</sup>)NR<sup>2</sup>R<sup>2a</sup>,  
 NHC(=NR<sup>2</sup>)NR<sup>2</sup>R<sup>2a</sup>, SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>SO<sub>2</sub>-C<sub>1-4</sub>  
 25 alkyl, NR<sup>2</sup>SO<sub>2</sub>R<sup>5</sup>, C(O)NHSO<sub>2</sub>-C<sub>1-4</sub> alkyl, S(O)<sub>p</sub>R<sup>5</sup>, 5-6  
 membered carbocycle substituted with 0-1 R<sup>5</sup>, and 5-6  
 membered heterocycle consisting of: carbon atoms and  
 1-4 heteroatoms selected from the group consisting of  
 N, O, and S(O)<sub>p</sub> substituted with 0-1 R<sup>5</sup>;

30 R<sup>4b</sup>, at each occurrence, is selected from H, =O, (CH<sub>2</sub>)<sub>r</sub>OR<sup>3</sup>,  
 (CH<sub>2</sub>)<sub>r</sub>-F, (CH<sub>2</sub>)<sub>r</sub>-Cl, (CH<sub>2</sub>)<sub>r</sub>-Br, (CH<sub>2</sub>)<sub>r</sub>-I, C<sub>1-4</sub> alkyl,  
 (CH<sub>2</sub>)<sub>r</sub>-CN, (CH<sub>2</sub>)<sub>r</sub>-NO<sub>2</sub>, (CH<sub>2</sub>)<sub>r</sub>NR<sup>3</sup>R<sup>3a</sup>, (CH<sub>2</sub>)<sub>r</sub>C(O)R<sup>3</sup>,

$(\text{CH}_2)_r\text{C}(\text{O})\text{OR}^{3c}$ ,  $\text{NR}^3\text{C}(\text{O})\text{R}^{3a}$ ,  $\text{C}(\text{O})\text{NR}^3\text{R}^{3a}$ ,  $\text{NR}^3\text{C}(\text{O})\text{NR}^3\text{R}^{3a}$ ,  
 $\text{C}(=\text{NR}^3)\text{NR}^3\text{R}^{3a}$ ,  $\text{NR}^3\text{C}(=\text{NR}^3)\text{NR}^3\text{R}^{3a}$ ,  $\text{SO}_2\text{NR}^3\text{R}^{3a}$ ,  $\text{NR}^3\text{SO}_2\text{NR}^3\text{R}^{3a}$ ,  
 $\text{NR}^3\text{SO}_2\text{-C}_{1-4}$  alkyl,  $\text{NR}^3\text{SO}_2\text{CF}_3$ ,  $\text{NR}^3\text{SO}_2\text{-phenyl}$ ,  $\text{S}(\text{O})_p\text{CF}_3$ ,  
 $\text{S}(\text{O})_p\text{-C}_{1-4}$  alkyl,  $\text{S}(\text{O})_p\text{-phenyl}$ ,  $(\text{CH}_2)_r\text{CF}_3$ , and  $(\text{CF}_2)_r\text{CF}_3$ ;

5

$\text{R}^5$ , at each occurrence, is selected from H,  $\text{C}_{1-6}$  alkyl, =O,  
 $(\text{CH}_2)_r\text{OR}^3$ , F, Cl, Br, I, -CN,  $\text{NO}_2$ ,  $(\text{CH}_2)_r\text{NR}^3\text{R}^{3a}$ ,  
 $(\text{CH}_2)_r\text{C}(\text{O})\text{R}^3$ ,  $(\text{CH}_2)_r\text{C}(\text{O})\text{OR}^{3c}$ ,  $\text{NR}^3\text{C}(\text{O})\text{R}^{3a}$ ,  $\text{C}(\text{O})\text{NR}^3\text{R}^{3a}$ ,  
 $\text{NR}^3\text{C}(\text{O})\text{NR}^3\text{R}^{3a}$ ,  $\text{CH}(=\text{NOR}^{3d})$ ,  $\text{C}(=\text{NR}^3)\text{NR}^3\text{R}^{3a}$ ,  
 $\text{NR}^3\text{C}(=\text{NR}^3)\text{NR}^3\text{R}^{3a}$ ,  $\text{SO}_2\text{NR}^3\text{R}^{3a}$ ,  $\text{NR}^3\text{SO}_2\text{NR}^3\text{R}^{3a}$ ,  $\text{NR}^3\text{SO}_2\text{-C}_{1-4}$   
 alkyl,  $\text{NR}^3\text{SO}_2\text{CF}_3$ ,  $\text{NR}^3\text{SO}_2\text{-phenyl}$ ,  $\text{S}(\text{O})_p\text{CF}_3$ ,  $\text{S}(\text{O})_p\text{-C}_{1-4}$   
 alkyl,  $\text{S}(\text{O})_p\text{-phenyl}$ ,  $(\text{CF}_2)_r\text{CF}_3$ , phenyl substituted with  
 0-2  $\text{R}^6$ , naphthyl substituted with 0-2  $\text{R}^6$ , and benzyl  
 substituted with 0-2  $\text{R}^6$ ;

15

$\text{R}^6$ , at each occurrence, is selected from H, OH,  $(\text{CH}_2)_r\text{OR}^2$ ,  
 halo,  $\text{C}_{1-4}$  alkyl, CN,  $\text{NO}_2$ ,  $(\text{CH}_2)_r\text{NR}^2\text{R}^{2a}$ ,  $(\text{CH}_2)_r\text{C}(\text{O})\text{R}^{2b}$ ,  
 $\text{NR}^2\text{C}(\text{O})\text{R}^{2b}$ ,  $\text{NR}^2\text{C}(\text{O})\text{NR}^2\text{R}^{2a}$ ,  $\text{C}(=\text{NH})\text{NH}_2$ ,  $\text{NHC}(=\text{NH})\text{NH}_2$ ,  
 $\text{SO}_2\text{NR}^2\text{R}^{2a}$ ,  $\text{NR}^2\text{SO}_2\text{NR}^2\text{R}^{2a}$ , and  $\text{NR}^2\text{SO}_2\text{C}_{1-4}$  alkyl;

20

$\text{R}^7$ , at each occurrence, is selected from H, OH,  $\text{C}_{1-4}$   
 alkoxy carbonyl,  $\text{C}_{6-10}$  aryloxy,  $\text{C}_{6-10}$  aryloxy carbonyl,  
 $\text{C}_{6-10}$  arylmethyl carbonyl,  $\text{C}_{1-4}$  alkyl carbonyloxy  $\text{C}_{1-4}$   
 alkoxy carbonyl,  $\text{C}_{6-10}$  aryl carbonyloxy  $\text{C}_{1-4}$   
 alkoxy carbonyl,  $\text{C}_{1-6}$  alkyl aminocarbonyl,  
 phenyl aminocarbonyl, and phenyl  $\text{C}_{1-4}$  alkoxy carbonyl;

25

$\text{R}^8$ , at each occurrence, is selected from H,  $\text{C}_{1-6}$  alkyl, and  
 $(\text{CH}_2)_n\text{-phenyl}$ ;

30

alternatively,  $\text{R}^7$  and  $\text{R}^8$ , when attached to the same nitrogen,  
 combine to form a 5-6 membered heterocyclic ring

consisting of carbon atoms and 0-2 additional heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>;

5 R<sup>9</sup>, at each occurrence, is selected from H, C<sub>1-6</sub> alkyl, and (CH<sub>2</sub>)<sub>n</sub>-phenyl;

n, at each occurrence, is selected from 0, 1, 2, and 3;

10 m, at each occurrence, is selected from 0, 1, and 2;

p, at each occurrence, is selected from 0, 1, and 2;

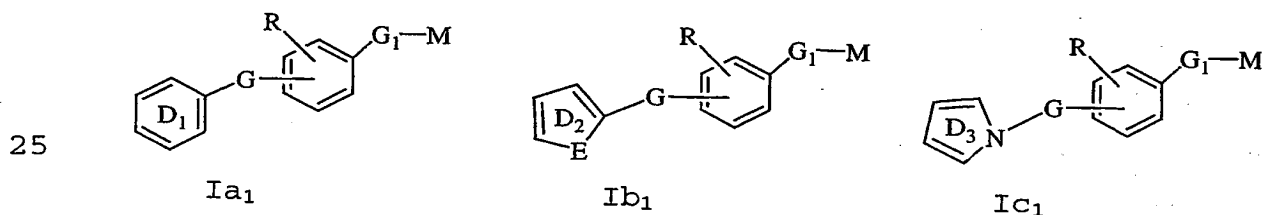
r, at each occurrence, is selected from 0, 1, 2, and 3;

15 s, at each occurrence, is selected from 0, 1, and 2; and,

t, at each occurrence, is selected from 0, 1, 2, and 3.

20

[2] In a preferred embodiment, the present invention provides a novel compound, wherein the compound is of formula Ia<sub>1</sub>-Ic<sub>1</sub>, wherein:



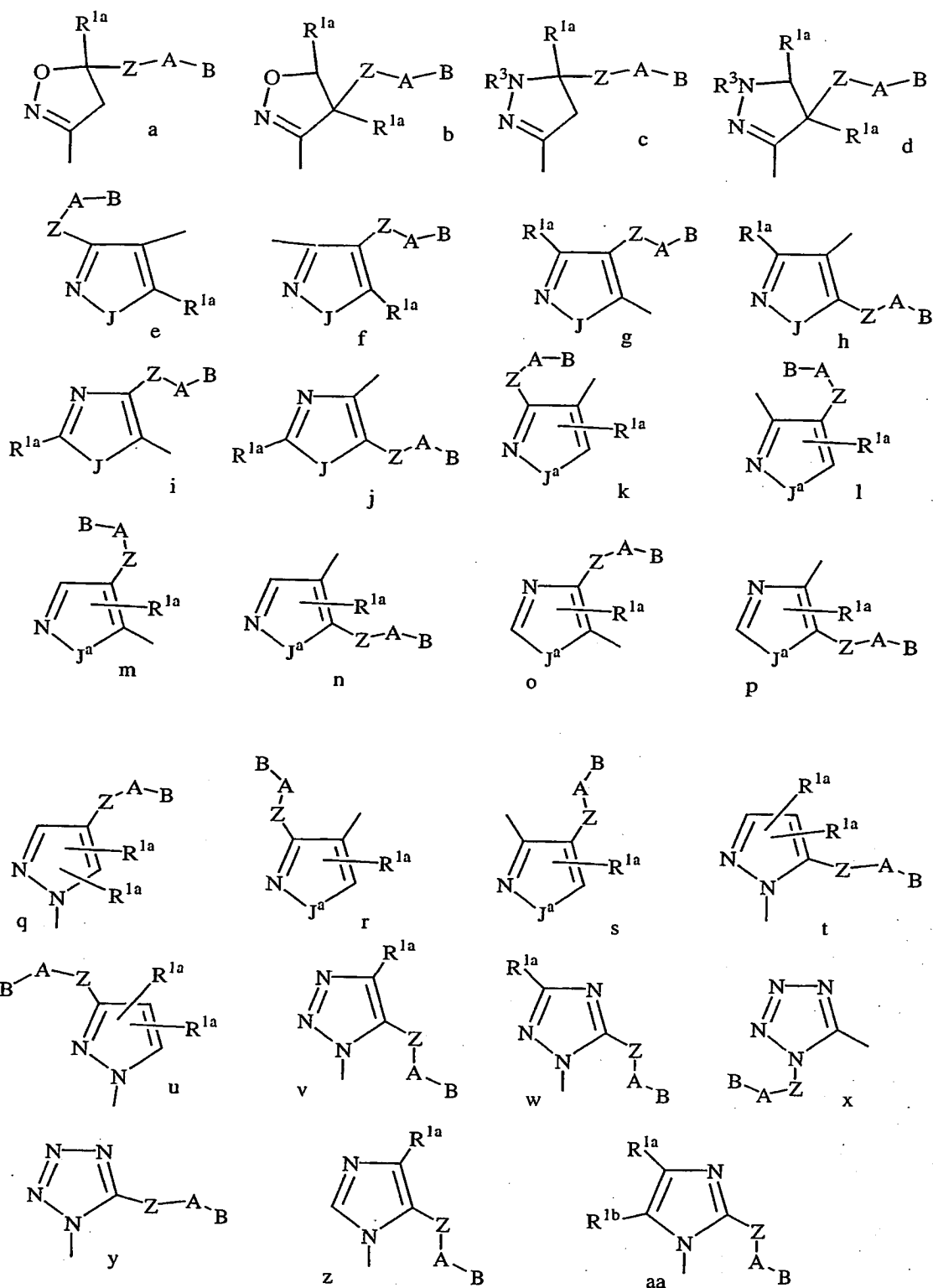
ring D<sub>2</sub> is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-R<sup>c</sup> and ring D<sub>2</sub> is substituted with 1 R<sup>a</sup> and 0-1 R<sup>b</sup>;

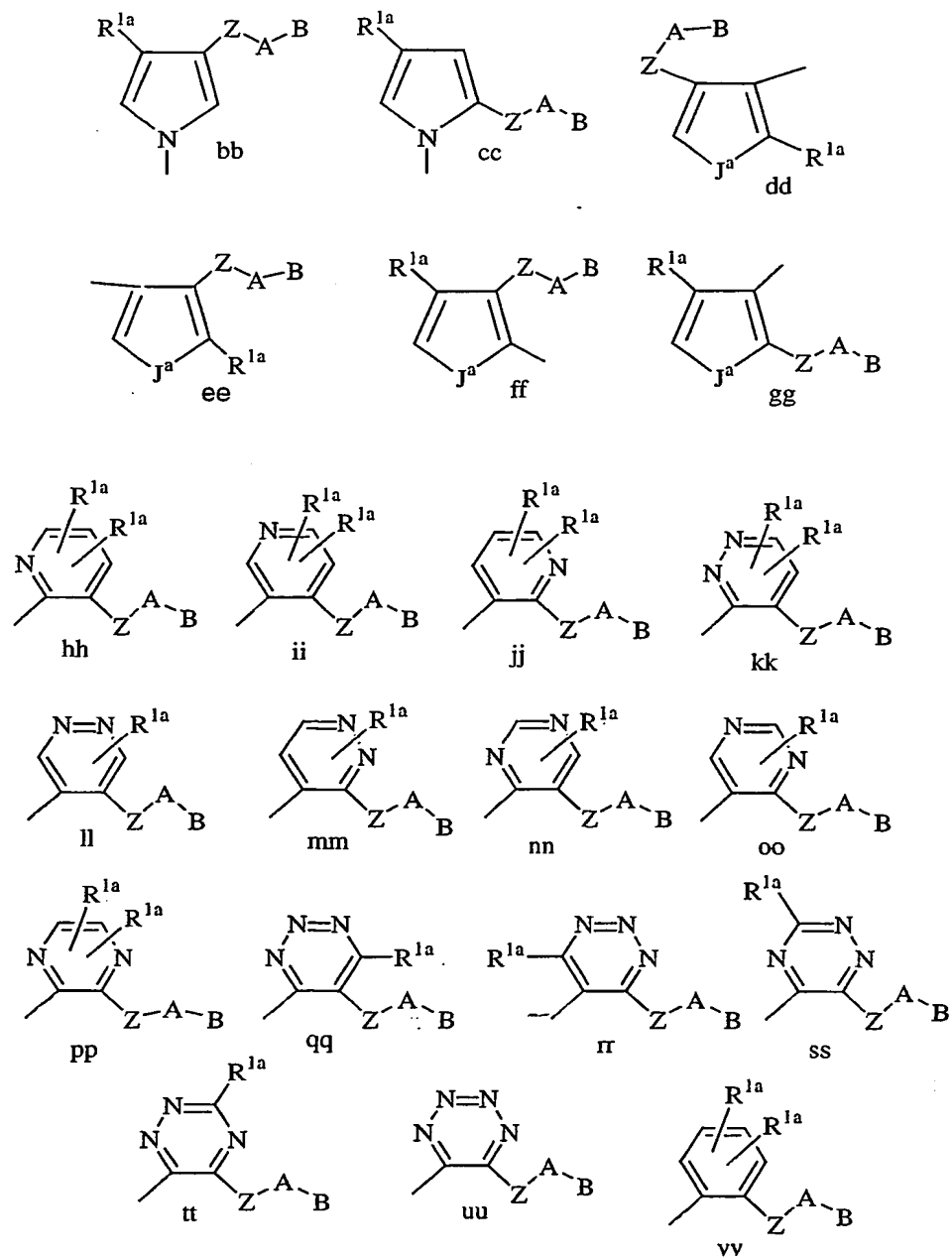
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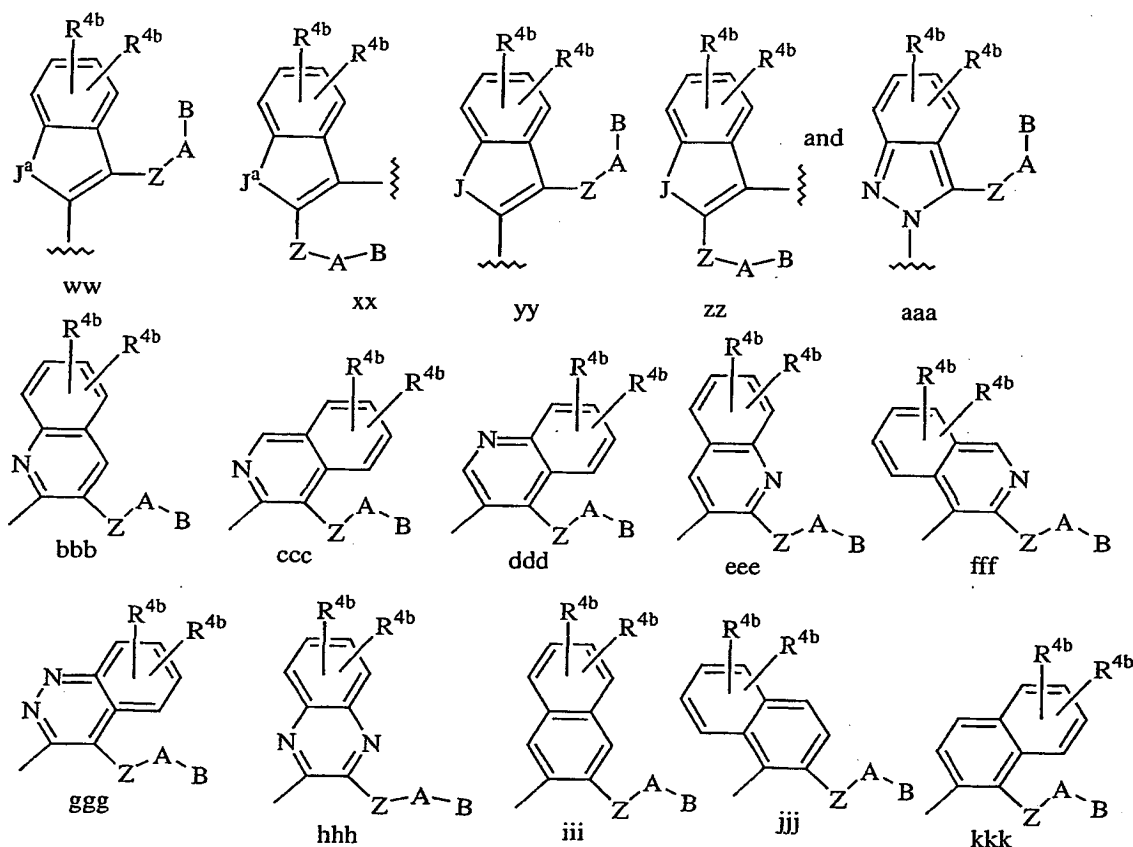
ring D<sub>3</sub> is a 5-membered heteroaromatic ring system comprising carbon atoms and from 0-3 additional N atoms and ring D<sub>3</sub> is substituted with 1 R<sup>a</sup> and 0-1 R<sup>b</sup>;

- 5 R is selected from H, Cl, F, Br, I, OH, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;
- 10 R<sup>a</sup> is selected from H, OH, SH, C<sub>1-3</sub> alkoxy, C<sub>1-3</sub> thioalkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;
- 15 R<sup>b</sup> is selected from H, C<sub>1-4</sub> alkyl, Cl, F, Br, I, OH, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;
- 20 R<sup>c</sup> is selected from H, C<sub>1-4</sub> alkyl, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;
- 25 G<sub>1</sub> is absent or is selected from CH<sub>2</sub>, C(O), O, NR<sup>3</sup>, S(O)<sub>p</sub>, CH<sub>2</sub>CH<sub>2</sub>, C(O)CH<sub>2</sub>, CH<sub>2</sub>C(O), OCH<sub>2</sub>, CH<sub>2</sub>O, NR<sup>3</sup>CH<sub>2</sub>, CH<sub>2</sub>NR<sup>3</sup>, S(O)<sub>p</sub>CH<sub>2</sub>, CH<sub>2</sub>S(O)<sub>p</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>, C(O)CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>C(O)CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>C(O), OCH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>OCH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>O, NR<sup>3</sup>CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>NR<sup>3</sup>CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NR<sup>3</sup>, S(O)<sub>p</sub>CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>S(O)<sub>p</sub>CH<sub>2</sub>, and CH<sub>2</sub>CH<sub>2</sub>S(O)<sub>p</sub>, and
- 30 provided that G<sub>1</sub>-M form other than a N-N, O-N, or S-N bond;

M is selected from the group:







J is O or S;

5 J<sup>a</sup> is NH or NR<sup>1a</sup>;

G<sub>1</sub> is absent or is selected from (CR<sup>3</sup>R<sup>3a</sup>)<sub>1-3</sub>,

(CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>C(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>O(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,

(CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>C(O)NR<sup>3</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,

10 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3</sup>C(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,

(CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(O)<sub>2</sub>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,

(CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(O)NR<sup>3</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, and (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(O)<sub>2</sub>NR<sup>3</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,

wherein u + w total 0, 1, or 2, provided that G<sub>1</sub> does

not form a N-N, N-O, N-S, NCH<sub>2</sub>N, NCH<sub>2</sub>O, or NCH<sub>2</sub>S bond

15 with either group to which it is attached;

A is selected from one of the following carbocyclic and heterocyclic systems which are substituted with 0-2 R<sup>4</sup>;



phenyl, piperidinyl, piperazinyl, pyridyl,  
pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl,  
pyrrolidinyl, oxazolyl, isoxazolyl, thiazolyl,  
isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl,  
5 thiadiazolyl, triazolyl, 1,2,3-oxadiazolyl,  
1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl,  
1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl,  
1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl,  
1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl,  
10 1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl,  
benzothiofuranyl, indolyl, benzimidazolyl,  
benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl,  
benzisothiazolyl, and isoindazolyl;

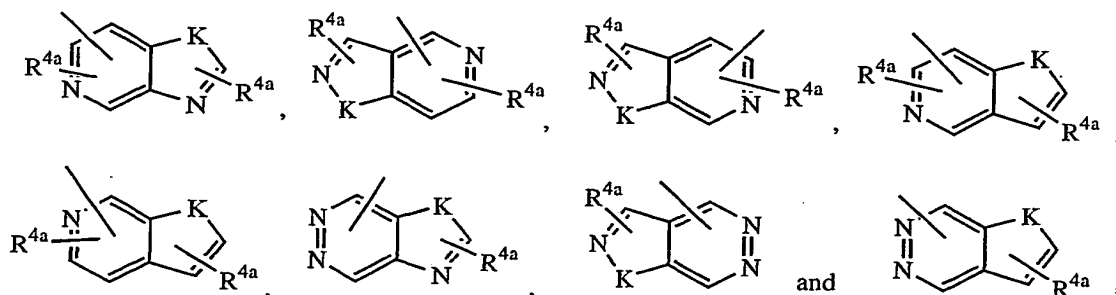
15 X is selected from  $-(CR^2R^{2a})_{1-4}-$ ,  $-C(O)-$ ,  $-C(=NR^{1c})-$ ,  
 $-CR^2(NR^{1c}R^2)-$ ,  $-C(O)CR^2R^{2a}-$ ,  $-CR^2R^{2a}C(O)-$ ,  $-C(O)NR^2-$ ,  
 $-NR^2C(O)-$ ,  $-C(O)NR^2CR^2R^{2a}-$ ,  $-NR^2C(O)CR^2R^{2a}-$ ,  
 $-CR^2R^{2a}C(O)NR^2-$ ,  $-CR^2R^{2a}NR^2C(O)-$ ,  $-NR^2C(O)NR^2-$ ,  $-NR^2-$ ,  
20  $-NR^2CR^2R^{2a}-$ ,  $-CR^2R^{2a}NR^2-$ , O,  $-CR^2R^{2a}O-$ , and  $-OCR^2R^{2a}-$ ;

Y is selected from one of the following carbocyclic and  
heterocyclic systems that are substituted with 0-2  $R^{4a}$ ;  
cyclopropyl, cyclopentyl, cyclohexyl, phenyl,  
piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl,  
25 morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl,  
oxazolyl, isoxazolyl, isoxazolinyl, thiazolyl,  
isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl,  
thiadiazolyl, triazolyl, 1,2,3-oxadiazolyl,  
1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl,  
30 1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl,  
1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl,  
1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl,  
1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl,  
benzothiofuranyl, indolyl, benzimidazolyl,

benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, and isoindazolyl;

alternatively, Y is selected from the following bicyclic

5 heteroaryl ring systems:



K is selected from O, S, NH, and N;

10 Z is selected from a bond, CH<sub>2</sub>O, OCH<sub>2</sub>, NH, CH<sub>2</sub>NH, NHCH<sub>2</sub>, CH<sub>2</sub>C(O), C(O)CH<sub>2</sub>, C(O)NH, NHC(O), CH<sub>2</sub>S(O)<sub>2</sub>, S(O)<sub>2</sub>(CH<sub>2</sub>), SO<sub>2</sub>NH, and NHSO<sub>2</sub>, provided that Z does not form a N-N, N-O, N-S, NCH<sub>2</sub>N, NCH<sub>2</sub>O, or NCH<sub>2</sub>S bond with either group to which it is attached;

15

R<sup>4</sup>, at each occurrence, is selected from H, =O, (CH<sub>2</sub>)<sub>r</sub>OR<sup>2</sup>, F, Cl, Br, I, C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, (CH<sub>2</sub>)<sub>r</sub>NR<sup>2</sup>R<sup>2a</sup>, C(O)R<sup>2c</sup>, NR<sup>2</sup>C(O)R<sup>2b</sup>, C(O)NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>C(O)NR<sup>2</sup>R<sup>2a</sup>, C(=NR<sup>2</sup>)NR<sup>2</sup>R<sup>2a</sup>, SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>SO<sub>2</sub>-C<sub>1-4</sub> alkyl, NR<sup>2</sup>SO<sub>2</sub>R<sup>5</sup>, S(O)<sub>p</sub>R<sup>5</sup>, CF<sub>3</sub>, NCH<sub>2</sub>R<sup>1c</sup>, OCH<sub>2</sub>R<sup>1c</sup>, SCH<sub>2</sub>R<sup>1c</sup>, N(CH<sub>2</sub>)<sub>2</sub>(CH<sub>2</sub>)<sub>t</sub>R<sup>1b</sup>, O(CH<sub>2</sub>)<sub>2</sub>(CH<sub>2</sub>)<sub>t</sub>R<sup>1b</sup>, S(CH<sub>2</sub>)<sub>2</sub>(CH<sub>2</sub>)<sub>t</sub>R<sup>1b</sup>, 5-6 membered carbocycle substituted with 0-1 R<sup>5</sup>, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub> substituted with 0-1 R<sup>5</sup>; and,

20

25

R<sup>4a</sup>, at each occurrence, is selected from H, =O, (CH<sub>2</sub>)<sub>r</sub>OR<sup>2</sup>, CF<sub>3</sub>, F, Br, Cl, C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, (CH<sub>2</sub>)<sub>r</sub>NR<sup>2</sup>R<sup>2a</sup>,

(CH<sub>2</sub>)<sub>r</sub>C(O)R<sup>2c</sup>, NR<sup>2</sup>C(O)R<sup>2b</sup>, C(O)NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>C(O)NR<sup>2</sup>R<sup>2a</sup>,  
C(=NR<sup>2</sup>)NR<sup>2</sup>R<sup>2a</sup>, NHC(=NR<sup>2</sup>)NR<sup>2</sup>R<sup>2a</sup>, SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>,  
NR<sup>2</sup>SO<sub>2</sub>-C<sub>1-4</sub> alkyl, NR<sup>2</sup>SO<sub>2</sub>R<sup>5</sup>, C(O)NHSO<sub>2</sub>-C<sub>1-4</sub> alkyl,  
S(O)<sub>p</sub>R<sup>5</sup>, 5-6 membered carbocycle substituted with 0-1  
5 R<sup>5</sup>, and 5-6 membered heterocycle consisting of: carbon  
atoms and 1-4 heteroatoms selected from the group  
consisting of N, O, and S(O)<sub>p</sub> substituted with 0-1 R<sup>5</sup>.

10 [3] In another preferred embodiment, the present invention  
provides a novel compound, wherein the compound is of  
formula Ib<sub>1</sub> or Ic<sub>1</sub>, wherein;

ring D<sub>2</sub> is a 5-membered heteroaromatic ring system  
15 comprising E, carbon atoms, and 0-2 N atoms, wherein E  
is selected from O, S, and N-R<sup>c</sup> and ring D<sub>2</sub> is  
substituted with 1 R<sup>a</sup> and 0-1 R<sup>b</sup>;

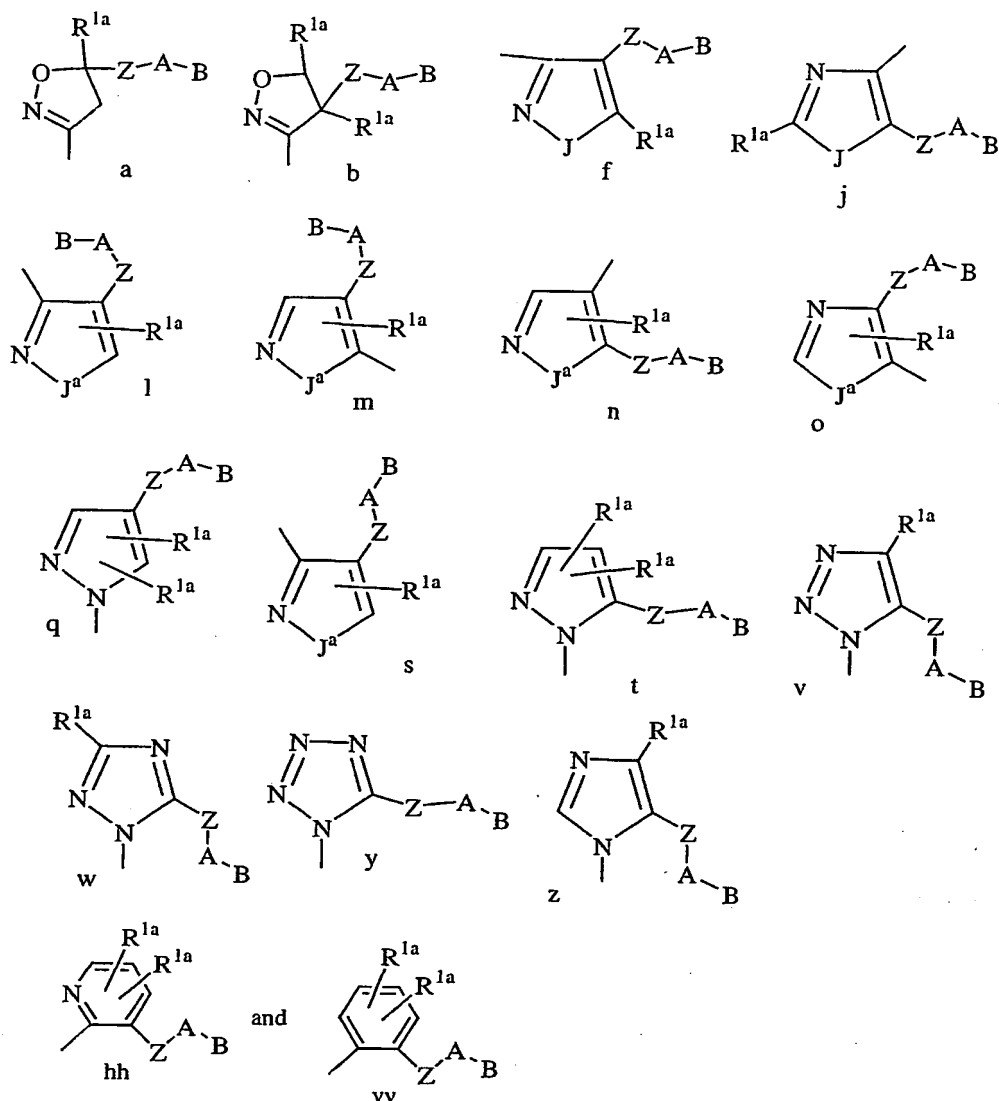
R is selected from H, Cl, F, Br, I, OH, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>,  
20 NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub>  
alkyl), and CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

R<sup>a</sup> is selected from H, OH, SH, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub>  
alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>N(C<sub>1-3</sub>  
25 alkyl)<sub>2</sub>;

R<sup>b</sup> is selected from H, C<sub>1-4</sub> alkyl, Cl, F, Br, I, OH, C<sub>1-3</sub>  
alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>,  
CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

30 R<sup>c</sup> is selected from H, C<sub>1-4</sub> alkyl, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub>  
alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and  
CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

M is selected from the group:



Y is selected from one of the following carbocyclic and heterocyclic systems which are substituted with 0-2  $R^{4a}$ ; phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazole, thiadiazole, triazole, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadiazole, 1,2,3-triazole, 1,2,4-triazole,

1,2,5-triazole, 1,3,4-triazole, benzofuran,  
benzothiofuran, indole, benzimidazole, benzimidazolone,  
benzoxazole, benzthiazole, indazole, benzisoxazole,  
benzisothiazole, and isoindazole;

5

Z is selected from a bond,  $\text{CH}_2\text{O}$ ,  $\text{OCH}_2$ ,  $\text{NH}$ ,  $\text{CH}_2\text{NH}$ ,  $\text{NHCH}_2$ ,  
 $\text{CH}_2\text{C}(\text{O})$ ,  $\text{C}(\text{O})\text{CH}_2$ ,  $\text{C}(\text{O})\text{NH}$ ,  $\text{NHC}(\text{O})$ ,  $\text{CH}_2\text{S}(\text{O})_2$ ,  $\text{S}(\text{O})_2(\text{CH}_2)$ ,  
 $\text{SO}_2\text{NH}$ , and  $\text{NHSO}_2$ , provided that Z does not form a N-N,  
N-O, N-S,  $\text{NCH}_2\text{N}$ ,  $\text{NCH}_2\text{O}$ , or  $\text{NCH}_2\text{S}$  bond with either group  
to which it is attached;

10

$\text{R}^4$ , at each occurrence, is selected from H,  $=\text{O}$ ,  $(\text{CH}_2)_r\text{OR}^2$ , F,  
Cl, Br, I,  $\text{C}_{1-4}$  alkyl, CN,  $\text{NO}_2$ ,  $(\text{CH}_2)_r\text{NR}^2\text{R}^{2a}$ ,  $\text{C}(\text{O})\text{R}^{2c}$ ,  
 $\text{NR}^2\text{C}(\text{O})\text{R}^{2b}$ ,  $\text{C}(\text{O})\text{NR}^2\text{R}^{2a}$ ,  $\text{NR}^2\text{C}(\text{O})\text{NR}^2\text{R}^{2a}$ ,  $\text{C}(=\text{NR}^2)\text{NR}^2\text{R}^{2a}$ ,  
 $\text{SO}_2\text{NR}^2\text{R}^{2a}$ ,  $\text{NR}^2\text{SO}_2\text{NR}^2\text{R}^{2a}$ ,  $\text{NR}^2\text{SO}_2\text{-C}_{1-4}$  alkyl,  $\text{NR}^2\text{SO}_2\text{R}^5$ ,  
 $\text{S}(\text{O})_p\text{R}^5$ ,  $\text{CF}_3$ , 5-6 membered carbocycle substituted with  
0-1  $\text{R}^5$ , and 5-6 membered heterocycle consisting of:  
carbon atoms and 1-4 heteroatoms selected from the  
group consisting of N, O, and  $\text{S}(\text{O})_p$  substituted with 0-1  
 $\text{R}^5$ ; and,

15

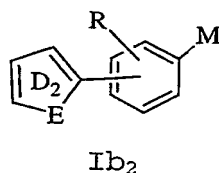
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$\text{R}^{4a}$ , at each occurrence, is selected from H,  $=\text{O}$ ,  $(\text{CH}_2)_r\text{OR}^2$ ,  
 $\text{CF}_3$ , F, Br, Cl,  $\text{C}_{1-4}$  alkyl, CN,  $\text{NO}_2$ ,  $(\text{CH}_2)_r\text{NR}^2\text{R}^{2a}$ ,  
 $(\text{CH}_2)_r\text{C}(\text{O})\text{R}^{2c}$ ,  $\text{NR}^2\text{C}(\text{O})\text{R}^{2b}$ ,  $\text{C}(\text{O})\text{NR}^2\text{R}^{2a}$ ,  $\text{NR}^2\text{C}(\text{O})\text{NR}^2\text{R}^{2a}$ ,  
 $\text{C}(=\text{NR}^2)\text{NR}^2\text{R}^{2a}$ ,  $\text{SO}_2\text{NR}^2\text{R}^{2a}$ ,  $\text{C}(\text{O})\text{NHSO}_2\text{-C}_{1-4}$  alkyl,  $\text{S}(\text{O})_p\text{R}^5$ ,  
5-6 membered carbocycle substituted with 0-1  $\text{R}^5$ , and 5-6  
membered heterocycle consisting of: carbon atoms and  
1-4 heteroatoms selected from the group consisting of  
N, O, and  $\text{S}(\text{O})_p$  substituted with 0-1  $\text{R}^5$ .

25

30

[4] In another preferred embodiment, the present invention  
provides a novel compound, wherein the compound is of  
formula  $\text{Ib}_2$ :



or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

5

ring D<sub>2</sub> is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-R<sup>c</sup> and ring D<sub>2</sub> is substituted with 1 R<sup>a</sup> and 0-1 R<sup>b</sup>;

10

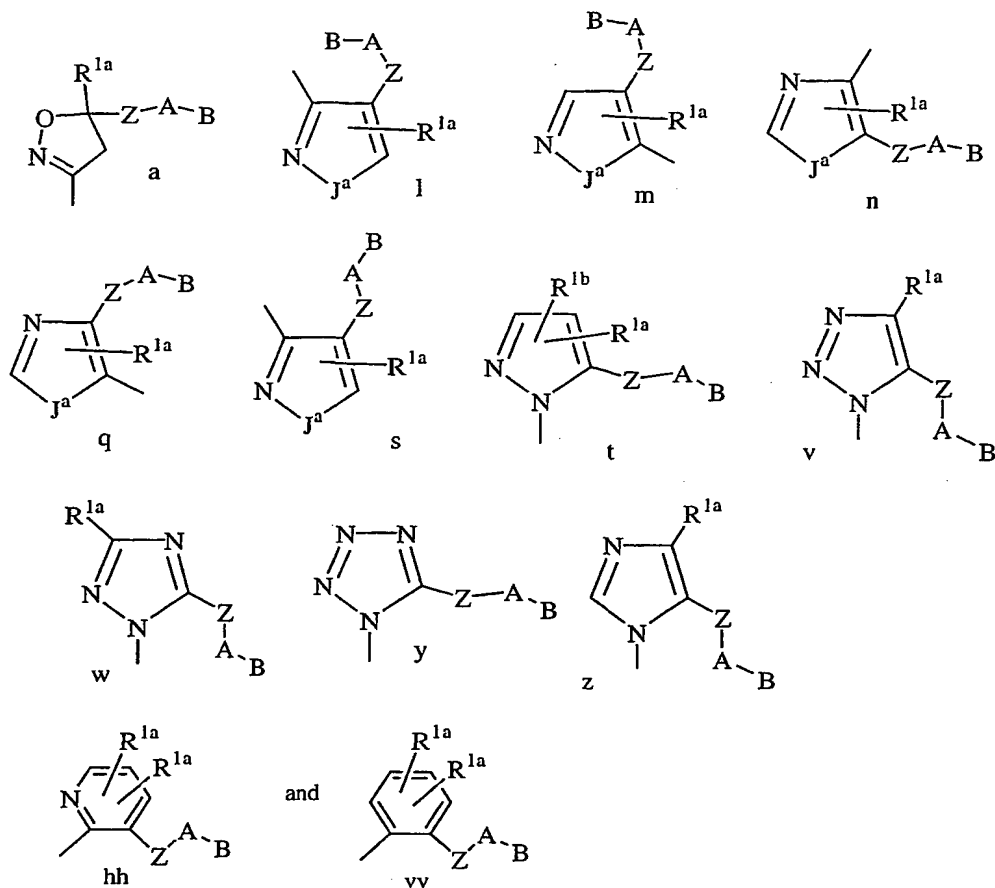
R is selected from H, Cl, F, Br, I, OH, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

15 R<sup>a</sup> is selected from H, OH, SH, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), and N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

R<sup>b</sup> is selected from H, C<sub>1-4</sub> alkyl, Cl, F, Br, I, OH, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

20

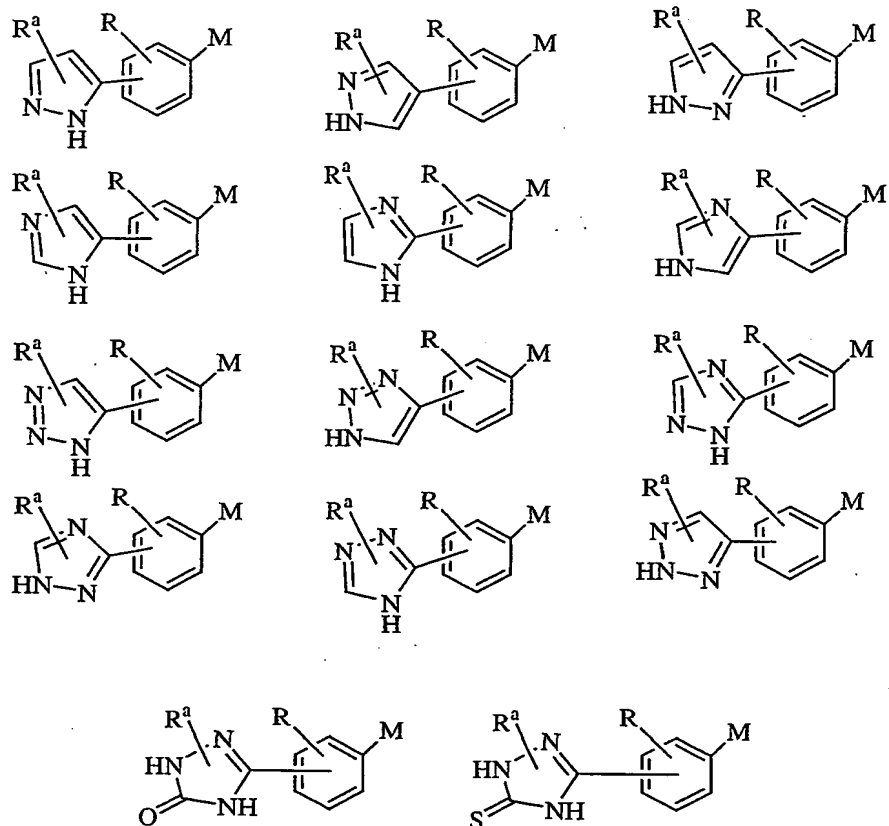
M is selected from the group:



G<sub>1</sub> is absent or is selected from CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>O, OCH<sub>2</sub>, NH, CH<sub>2</sub>NH, NHCH<sub>2</sub>, CH<sub>2</sub>C(O), C(O)CH<sub>2</sub>, C(O)NH, NHC(O),

5 CH<sub>2</sub>S(O)<sub>2</sub>, S(O)<sub>2</sub>(CH<sub>2</sub>), SO<sub>2</sub>NH, and NHSO<sub>2</sub>, provided that G<sub>1</sub> does not form a N-N, N-O, N-S, NCH<sub>2</sub>N, NCH<sub>2</sub>O, or NCH<sub>2</sub>S bond with either group to which it is attached.

10 [5] In another preferred embodiment, the present invention provides a novel compound, wherein the compound is selected from one of the formulas:



5 or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

$G_1$  is absent;

10 A is selected from phenyl, piperidinyl, pyridyl, and pyrimidyl, and is substituted with 0-2  $R^4$ ; and,

B is selected from phenyl, pyrrolidino, N-pyrrolidino-carbonyl, morpholino, N-morpholino-carbonyl, 1,2,3-  
 15 triazolyl, imidazolyl, and benzimidazolyl, and is substituted with 0-1  $R^{4a}$ ;

$R^2$ , at each occurrence, is selected from H,  $CH_3$ ,  $CH_2CH_3$ , cyclopropylmethyl, cyclobutyl, and cyclopentyl;

20



R<sup>2a</sup>, at each occurrence, is selected from H, CH<sub>3</sub>, and CH<sub>2</sub>CH<sub>3</sub>;

alternatively, R<sup>2</sup> and R<sup>2a</sup>, together with the atom to which they are attached, combine to form pyrrolidine

5 substituted with 0-2 R<sup>4b</sup> or piperidine substituted with 0-2 R<sup>4b</sup>;

R<sup>4</sup>, at each occurrence, is selected from OH, OR<sup>2</sup>, (CH<sub>2</sub>)OR<sup>2</sup>, (CH<sub>2</sub>)<sub>2</sub>OR<sup>2</sup>, F, Br, Cl, I, C<sub>1-4</sub> alkyl, NR<sup>2</sup>R<sup>2a</sup>, (CH<sub>2</sub>)NR<sup>2</sup>R<sup>2a</sup>,  
10 (CH<sub>2</sub>)<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, CF<sub>3</sub>, and (CF<sub>2</sub>)CF<sub>3</sub>;

R<sup>4a</sup> is selected from C<sub>1-4</sub> alkyl, CF<sub>3</sub>, OR<sup>2</sup>, (CH<sub>2</sub>)OR<sup>2</sup>, (CH<sub>2</sub>)<sub>2</sub>OR<sup>2</sup>, NR<sup>2</sup>R<sup>2a</sup>, (CH<sub>2</sub>)NR<sup>2</sup>R<sup>2a</sup>, (CH<sub>2</sub>)<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, SR<sup>5</sup>, S(O)R<sup>5</sup>, S(O)<sub>2</sub>R<sup>5</sup>, SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, and 1-CF<sub>3</sub>-tetrazol-2-yl;

15 R<sup>4b</sup>, at each occurrence, is selected from H, CH<sub>3</sub>, and OH;

R<sup>5</sup>, at each occurrence, is selected from CF<sub>3</sub>, C<sub>1-6</sub> alkyl, phenyl, and benzyl; and,

20 r, at each occurrence, is selected from 0, 1, and 2.

[6] In another preferred embodiment, the present invention  
25 provides a novel compound, wherein;

A is selected from the group: phenyl, piperidinyl, 2-pyridyl, 3-pyridyl, 2-pyrimidyl, 2-Cl-phenyl, 3-Cl-phenyl, 2-F-phenyl, 3-F-phenyl, 2-methylphenyl, 2-aminophenyl, and 2-methoxyphenyl; and,

30 B is selected from the group: 2-(aminosulfonyl)phenyl, 2-(methylaminosulfonyl)phenyl, 1-pyrrolidinocarbonyl, 2-(methylsulfonyl)phenyl, 2-(N,N-

dimethylaminomethyl)phenyl, 2-(N-methylaminomethyl)phenyl, 2-(N-ethyl-N-methylaminomethyl)phenyl, 2-(N-pyrrolidinylmethyl)phenyl, 1-methyl-2-imidazolyl, 2-methyl-1-imidazolyl, 2-(dimethylaminomethyl)-1-imidazolyl, 2-(methylaminomethyl)-1-imidazolyl, 2-(N-(cyclopropylmethyl)aminomethyl)phenyl, 2-(N-(cyclobutyl)aminomethyl)phenyl, 2-(N-(cyclopentyl)aminomethyl)phenyl, 2-(N-(4-hydroxypiperidinyl)methyl)phenyl, and 2-(N-(3-hydroxypyrrolidinyl)methyl)phenyl.

[7] In another preferred embodiment, the present invention provides a novel compound selected from the group:

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-5-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-5-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-5-[(2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

5 1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

10 1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

15 1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

20 1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

25 1-[3-(2'-Amino-3',4'-thiadiazol-5'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

30 1-[3-(2'-Amino-3',4'-thiadiazol-5'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(2'-Amino-3',4'-thiadiazol-5'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-5-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl]aminocarbonyl]pyrazole;

5

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-5-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl]aminocarbonyl]pyrazole;

10 1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

15 1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

20 1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

25 1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

30 1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(5-Amino-1,3,4-oxadiazol-2-yl)phenyl]-N-{2'-  
[(dimethylamino)methyl]-3-fluoro-1,1'-biphenyl-4-yl}-3-  
(trifluoromethyl)-1H-pyrazole-5-carboxamide;

5 1-[3-(5-Amino-1,3,4-oxadiazol-2-yl)phenyl]-N-(3-fluoro-2'-  
{[(3S)-3-hydroxy-1-pyrrolidinyl]methyl}-1,1'-biphenyl-  
4-yl)-3-(trifluoromethyl)-1H-pyrazole-5-carboxamide;  
and,

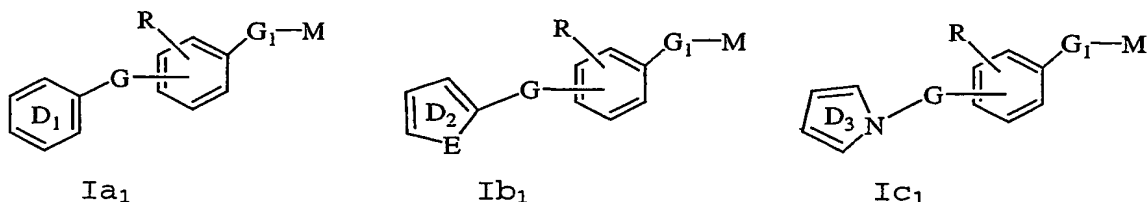
10 1-[3-(5-Amino-1,3,4-oxadiazol-2-yl)phenyl]-N-(3-fluoro-2'-  
{[(3S)-3-hydroxy-1-pyrrolidinyl]methyl}-1,1'-biphenyl-  
4-yl)-5-(trifluoromethyl)-1H-pyrazole-3-carboxamide;

or a pharmaceutically acceptable salt thereof.

15

In another embodiment, the present invention provides a  
novel compound, wherein the compound is of formula Ia<sub>1</sub>-Ic<sub>1</sub>,  
wherein:

20



ring D<sub>2</sub> is a 5-membered heteroaromatic ring system

25 comprising E, carbon atoms, and 0-2 N atoms, wherein E  
is selected from O, S, and N-R<sup>c</sup> and ring D<sub>2</sub> is  
substituted with 1 R<sup>a</sup> and 0-1 R<sup>b</sup>;

ring D<sub>3</sub> is a 5-membered heteroaromatic ring system

30 comprising carbon atoms and from 0-3 additional N atoms  
and ring D<sub>3</sub> is substituted with 1 R<sup>a</sup> and 0-1 R<sup>b</sup>;

R is selected from H, Cl, F, Br, I, OH, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

5

R<sup>a</sup> is selected from H, OH, SH, C<sub>1-3</sub> alkoxy, C<sub>1-3</sub> thioalkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

10

R<sup>b</sup> is selected from H, C<sub>1-4</sub> alkyl, Cl, F, Br, I, OH, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

15

R<sup>c</sup> is selected from H, C<sub>1-4</sub> alkyl, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>; and,

20

G<sub>1</sub> is absent or is selected from CH<sub>2</sub>, C(O), O, NR<sup>3</sup>, S(O)<sub>p</sub>, CH<sub>2</sub>CH<sub>2</sub>, C(O)CH<sub>2</sub>, CH<sub>2</sub>C(O), OCH<sub>2</sub>, CH<sub>2</sub>O, NR<sup>3</sup>CH<sub>2</sub>, CH<sub>2</sub>NR<sup>3</sup>, S(O)<sub>p</sub>CH<sub>2</sub>, CH<sub>2</sub>S(O)<sub>p</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>, C(O)CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>C(O)CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>C(O), OCH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>OCH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>O, NR<sup>3</sup>CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>NR<sup>3</sup>CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NR<sup>3</sup>, S(O)<sub>p</sub>CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>S(O)<sub>p</sub>CH<sub>2</sub>, and CH<sub>2</sub>CH<sub>2</sub>S(O)<sub>p</sub>, and provided that G<sub>1</sub>-M form other than a N-N, O-N, or S-N bond.

25

30 In another embodiment, the present invention provides a novel compound, wherein the compound is of formula Ib<sub>1</sub> or Ic<sub>1</sub>, wherein;

ring D<sub>2</sub> is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-R<sup>c</sup> and ring D<sub>2</sub> is substituted with 1 R<sup>a</sup> and 0-1 R<sup>b</sup>;

5

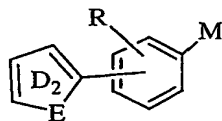
R is selected from H, Cl, F, Br, I, OH, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

10 R<sup>a</sup> is selected from H, OH, SH, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

15 R<sup>b</sup> is selected from H, C<sub>1-4</sub> alkyl, Cl, F, Br, I, OH, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>; and,

20 R<sup>c</sup> is selected from H, C<sub>1-4</sub> alkyl, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>.

In another embodiment, the present invention provides a novel compound, wherein the compound is of formula Ib<sub>2</sub>:



25

Ib<sub>2</sub>

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

30 ring D<sub>2</sub> is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E

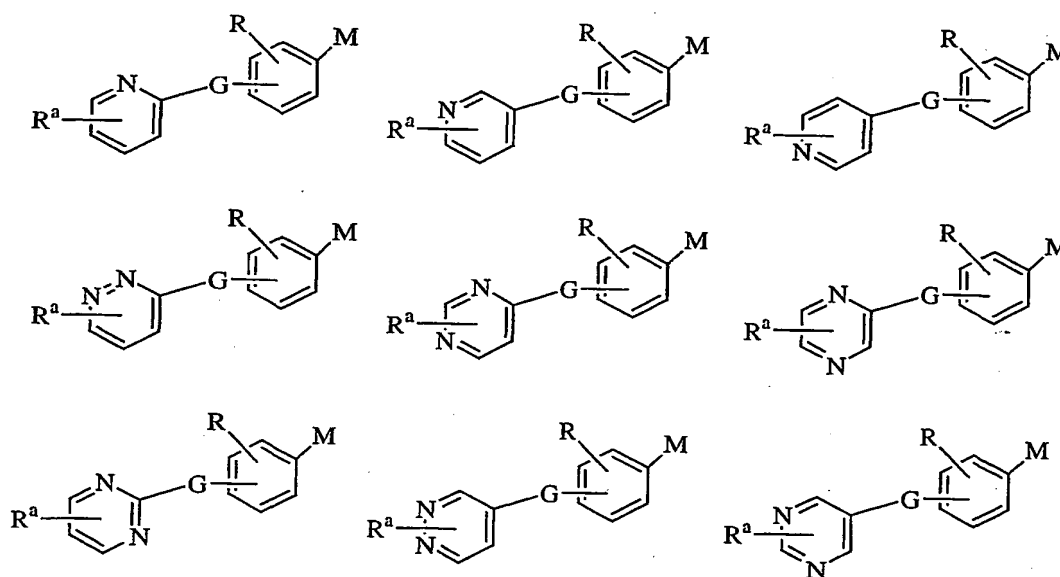
is selected from O, S, and N-R<sup>C</sup> and ring D<sub>2</sub> is substituted with 1 R<sup>a</sup> and 0-1 R<sup>b</sup>;

R is selected from H, Cl, F, Br, I, OH, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>,  
 5 NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

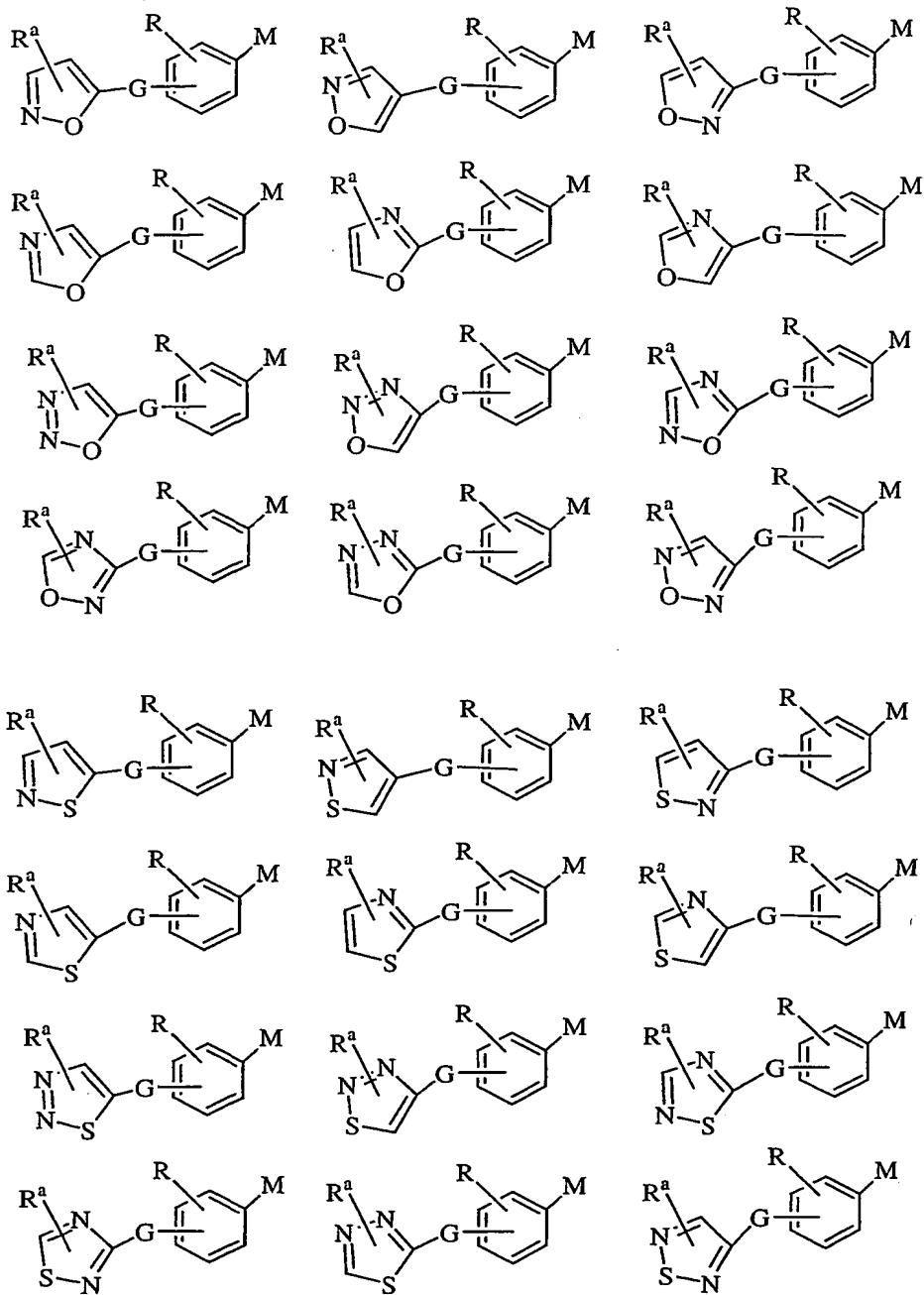
R<sup>a</sup> is selected from H, OH, SH, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), and N(C<sub>1-3</sub> alkyl)<sub>2</sub>; and,

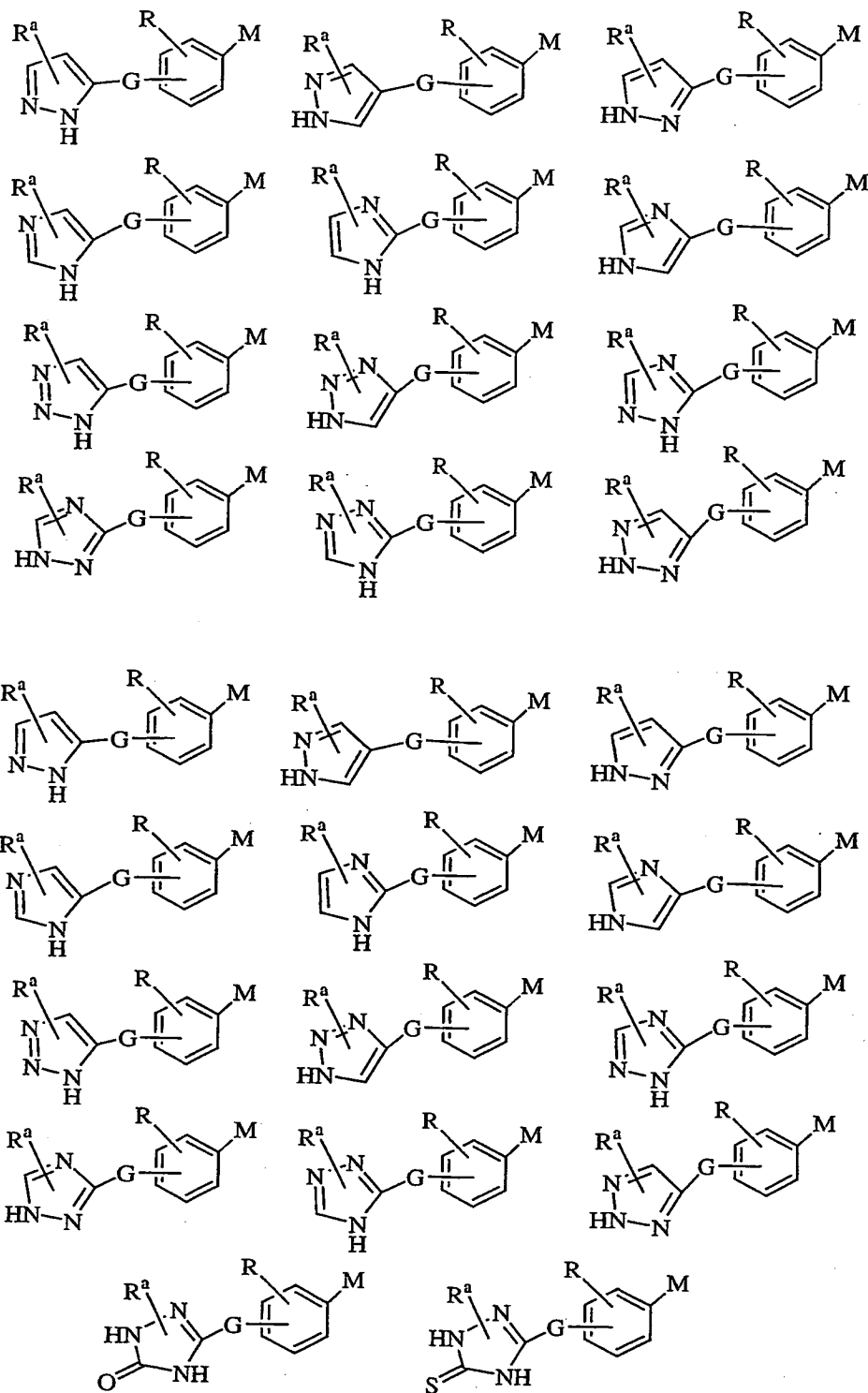
10 R<sup>b</sup> is selected from H, C<sub>1-4</sub> alkyl, Cl, F, Br, I, OH, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>.

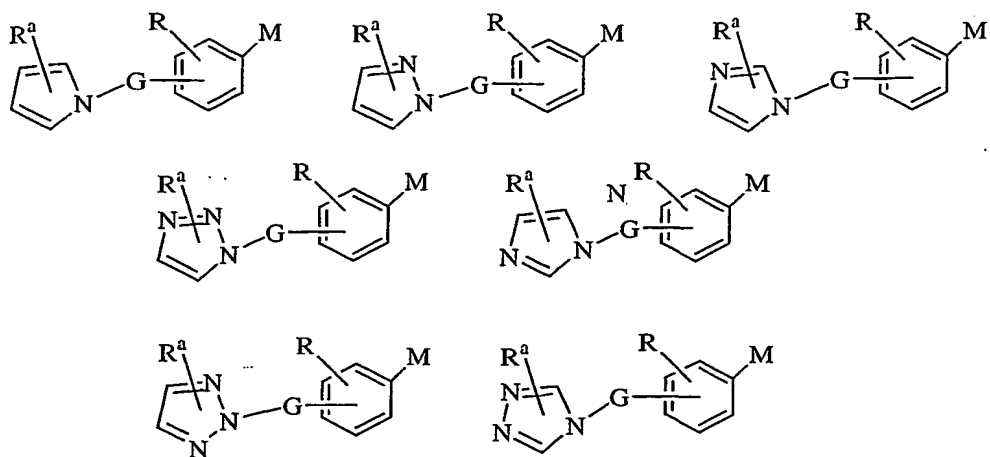
15 In another embodiment, the present invention provides a novel compound selected from one of the formulas:







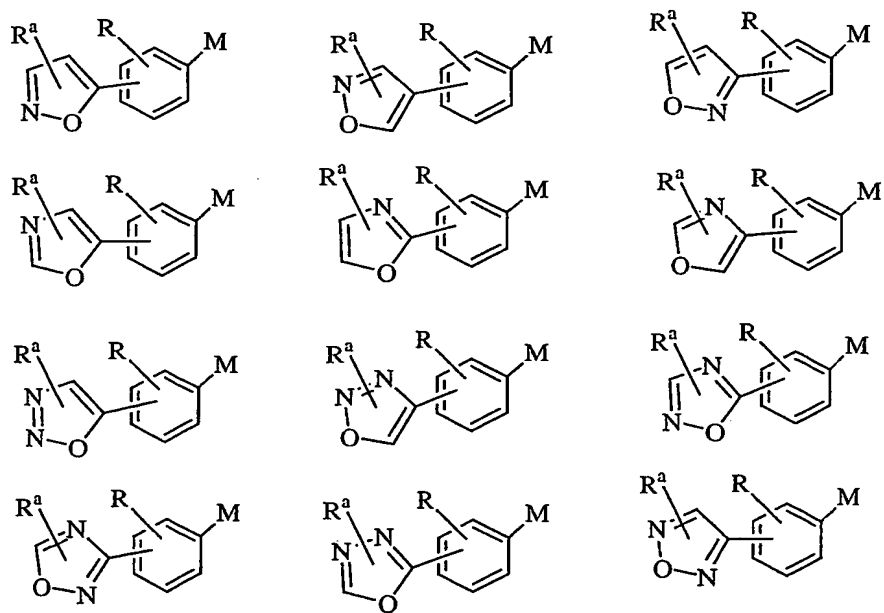




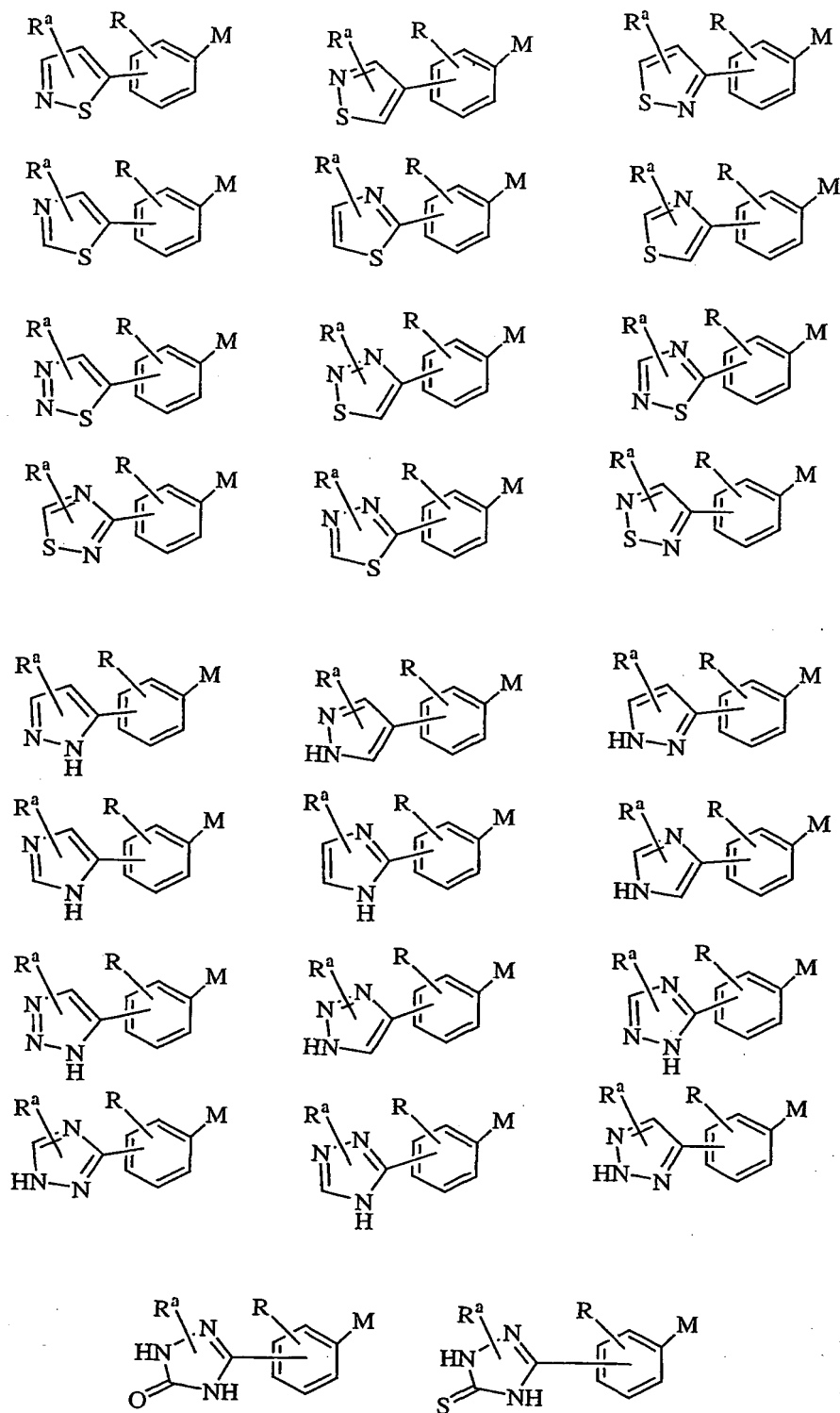
or a stereoisomer or pharmaceutically acceptable salt thereof.

5

In another embodiment, the present invention provides a novel compound selected from one of the formulas:



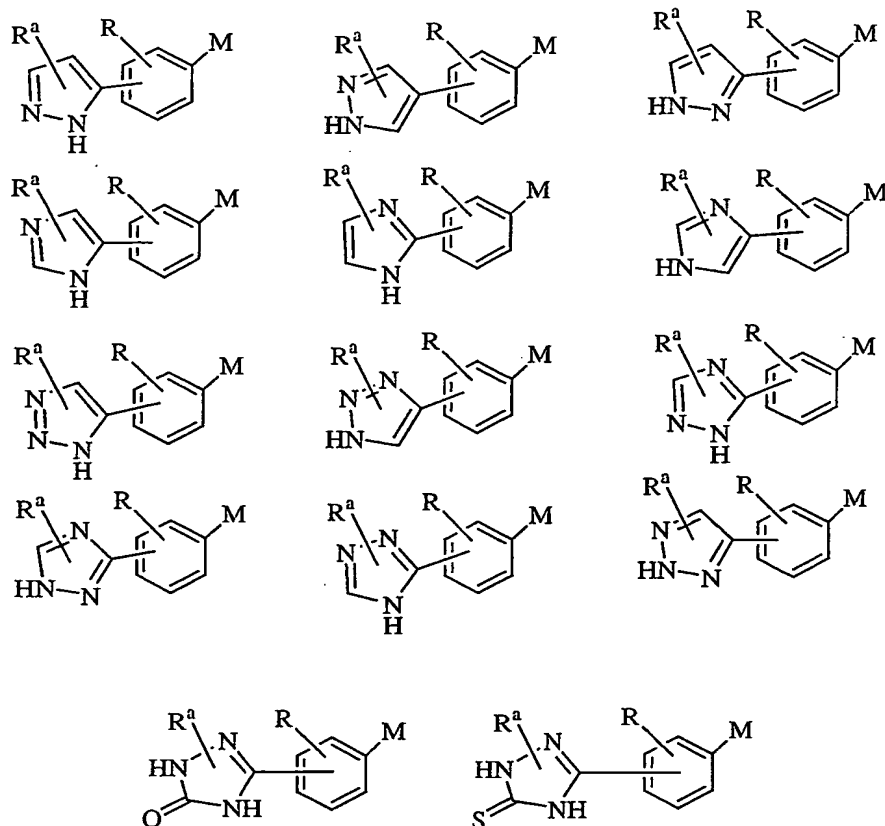
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5

or a stereoisomer or pharmaceutically acceptable salt thereof.

In another embodiment, the present invention provides a novel compound selected from one of the formulas:

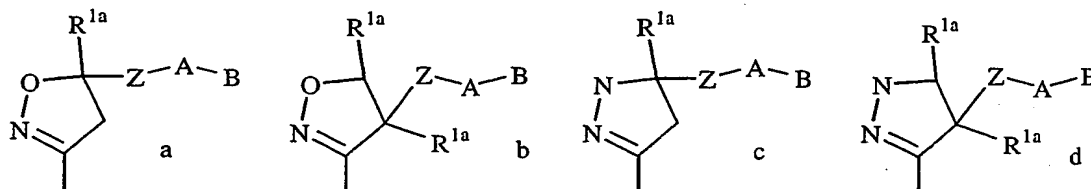


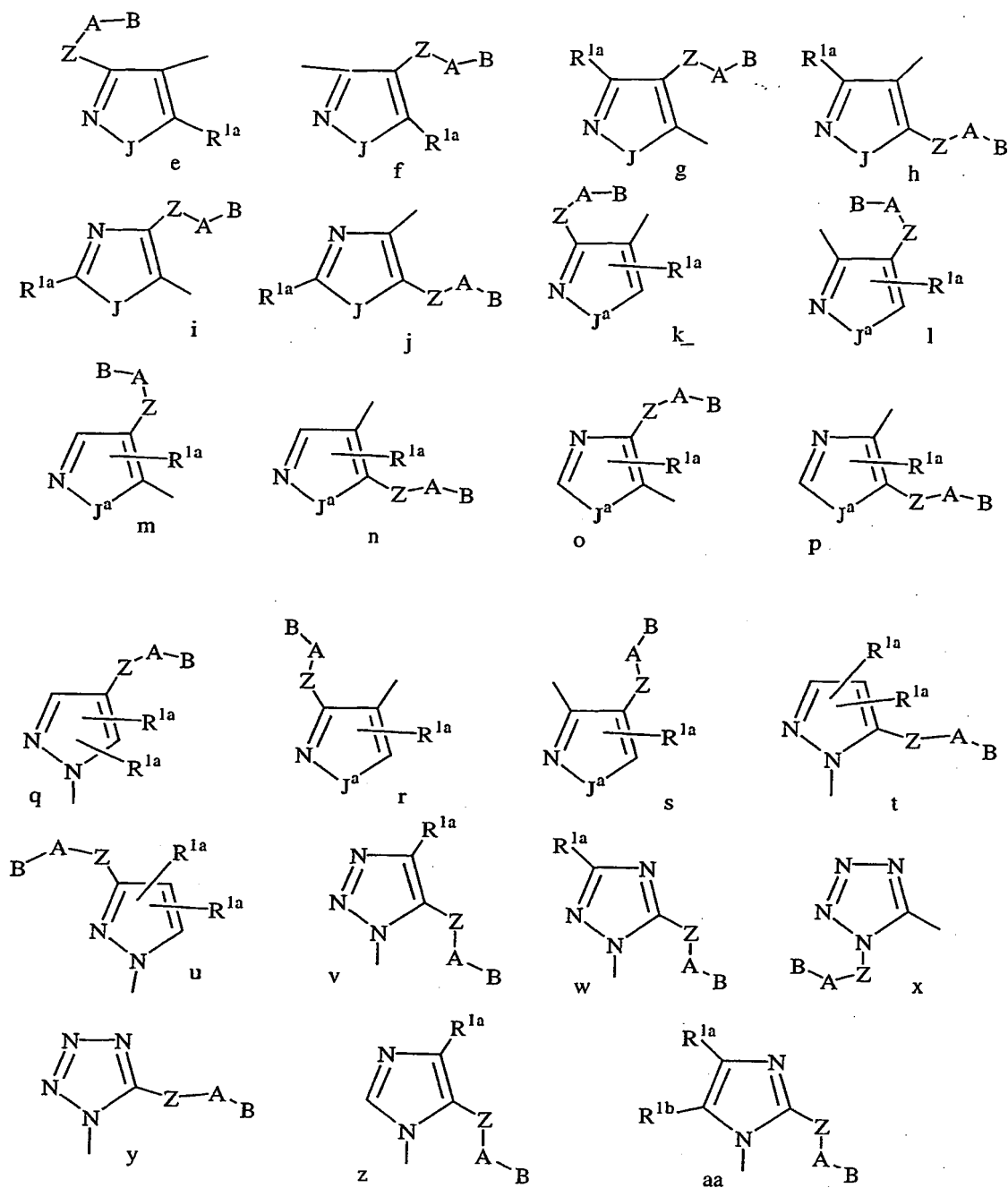
or a stereoisomer or pharmaceutically acceptable salt thereof.

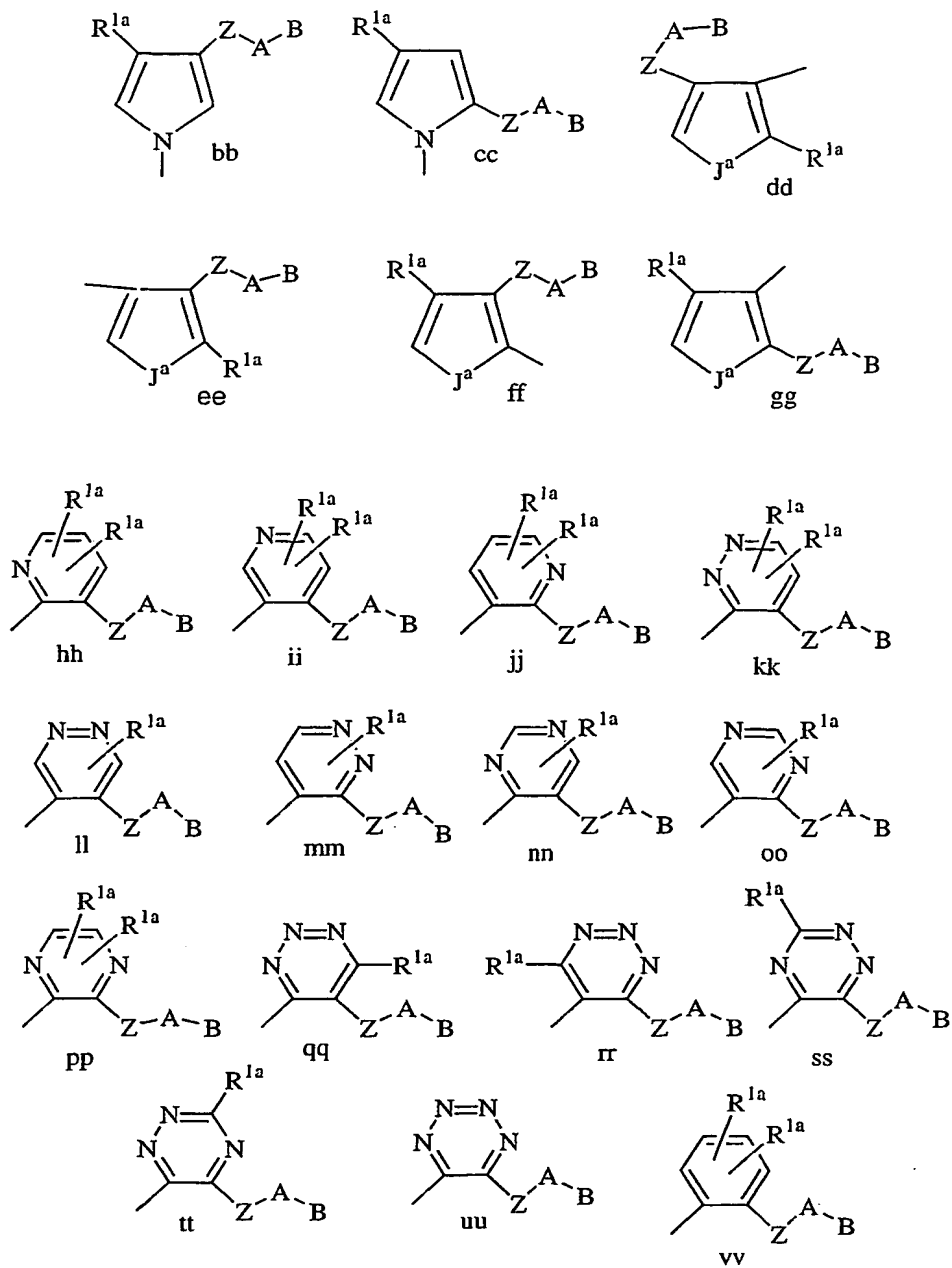
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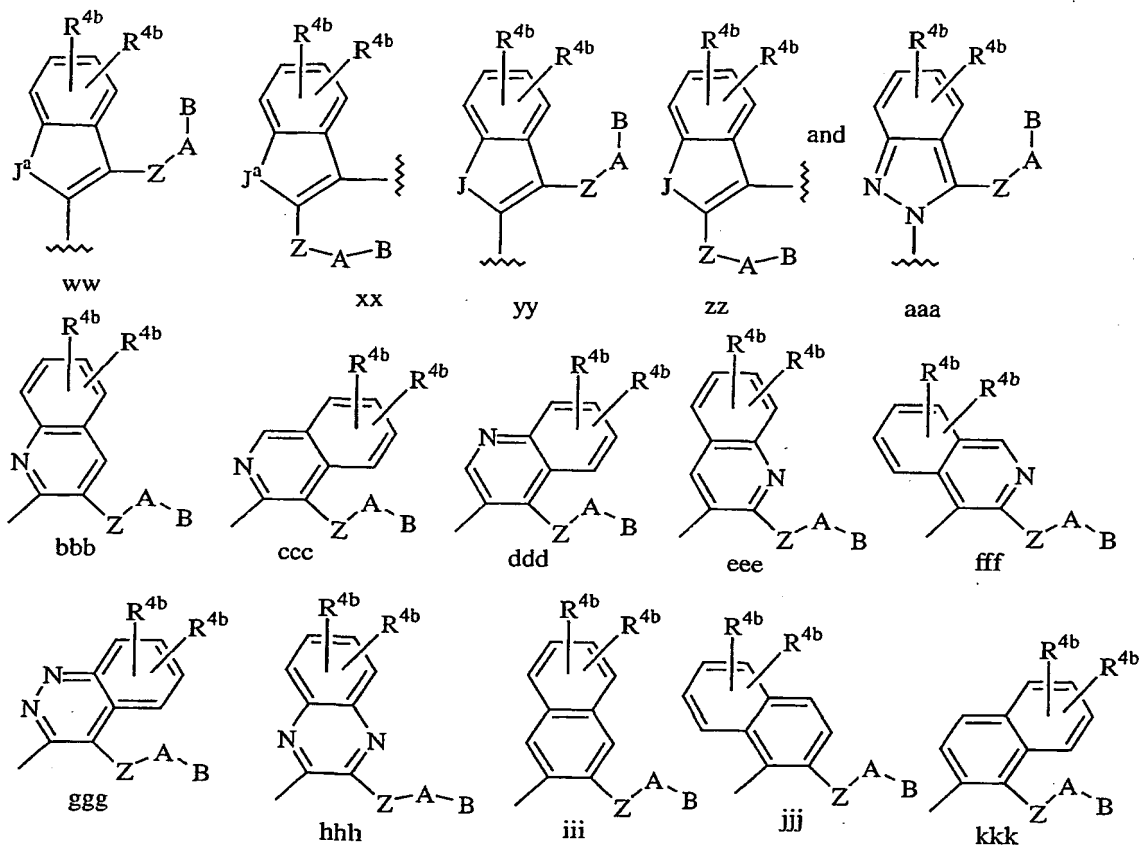
In another embodiment, the present invention provides a novel compound wherein M is selected from the group:

15









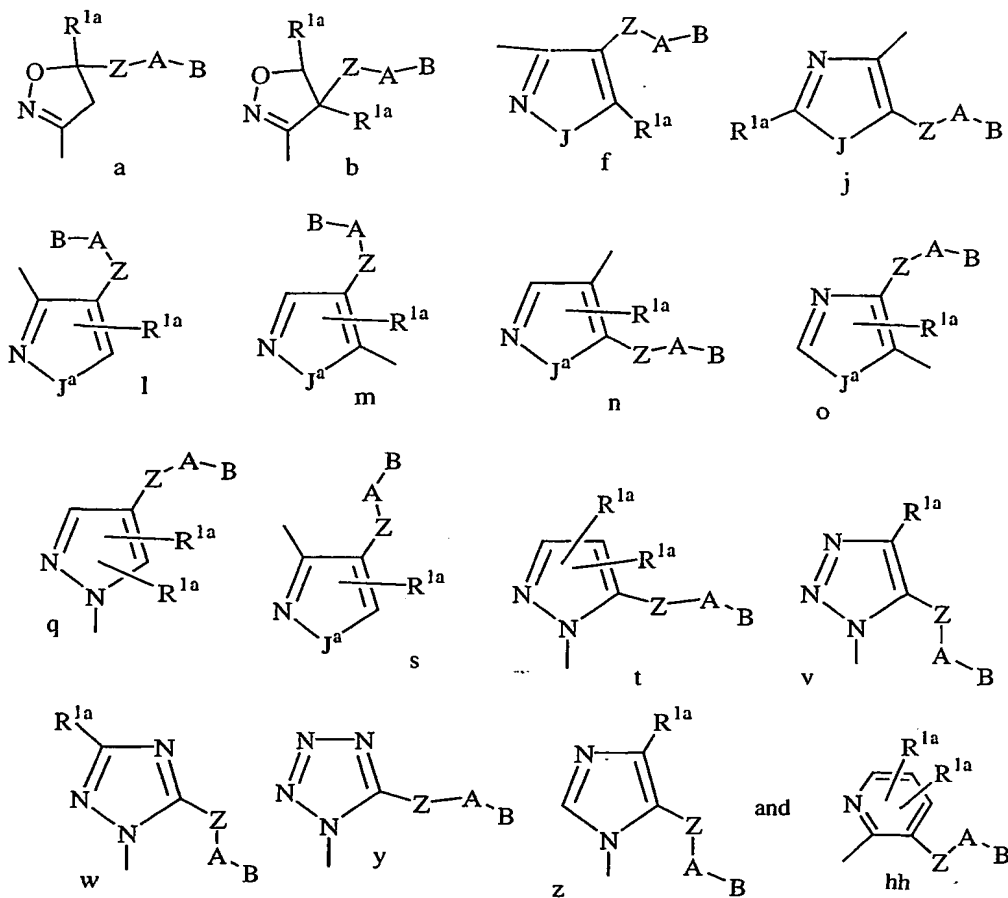
J is O or S; and,

5 J<sup>a</sup> is NH or NR<sup>1a</sup>.

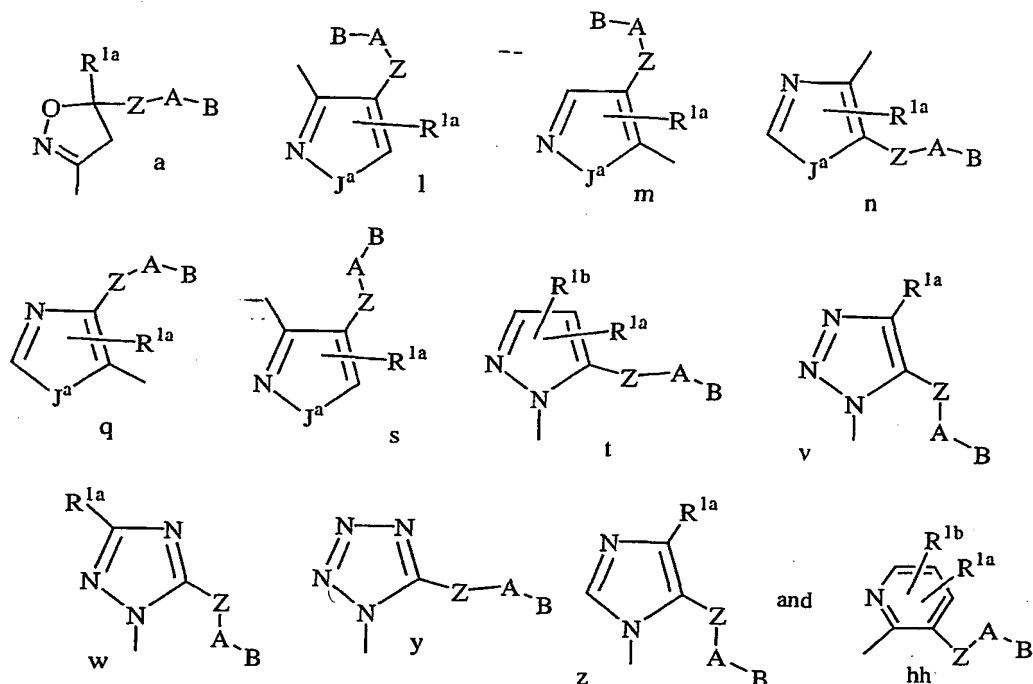
In another embodiment, the present invention provides a novel compound wherein M is selected from the group:

10





In another embodiment, the present invention provides a  
 5 novel compound wherein M is selected from the group:



In another embodiment, the present invention provides a novel compound wherein A is selected from one of the following carbocyclic and heterocyclic systems that are substituted with 0-2 R<sup>4</sup>;

phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, and isoindazolyl;

In another embodiment, the present invention provides a novel compound wherein A is selected from phenyl, piperidinyl, pyridyl, and pyrimidyl, and is substituted with 0-2 R<sup>4</sup>.

5

In another embodiment, the present invention provides a novel compound wherein A is selected from the group: phenyl, piperidinyl, 2-pyridyl, 3-pyridyl, 2-pyrimidyl, 2-Cl-phenyl, 3-Cl-phenyl, 2-F-phenyl, 3-F-phenyl, 2-methylphenyl, 2-aminophenyl, and 2-methoxyphenyl.

In another embodiment, the present invention provides a novel compound wherein:

B is selected from: H, Y, and X-Y, provided that Z and B are attached to different atoms on A;

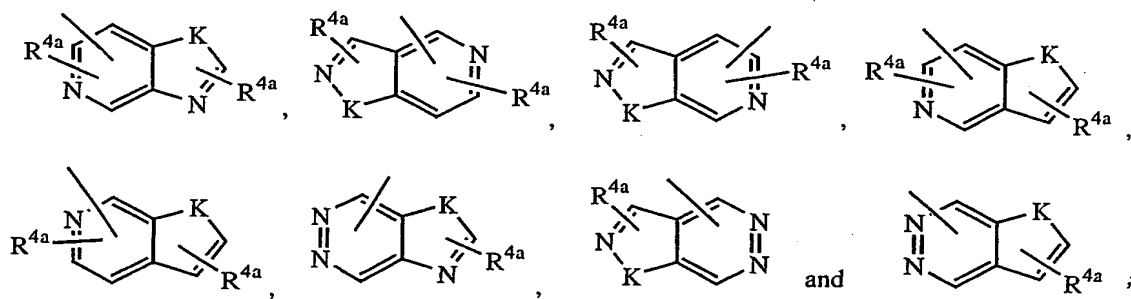
X is selected from -(CR<sup>2</sup>R<sup>2a</sup>)<sub>1-4</sub>-, -C(O)-, -C(=NR<sup>1c</sup>)-, -CR<sup>2</sup>(NR<sup>1c</sup>R<sup>2</sup>)-, -C(O)CR<sup>2</sup>R<sup>2a</sup>-, -CR<sup>2</sup>R<sup>2a</sup>C(O)-, -C(O)NR<sup>2</sup>-, -NR<sup>2</sup>C(O)-, -C(O)NR<sup>2</sup>CR<sup>2</sup>R<sup>2a</sup>-, -NR<sup>2</sup>C(O)CR<sup>2</sup>R<sup>2a</sup>-, -CR<sup>2</sup>R<sup>2a</sup>C(O)NR<sup>2</sup>-, -CR<sup>2</sup>R<sup>2a</sup>NR<sup>2</sup>C(O)-, -NR<sup>2</sup>C(O)NR<sup>2</sup>-, -NR<sup>2</sup>-, -NR<sup>2</sup>CR<sup>2</sup>R<sup>2a</sup>-, -CR<sup>2</sup>R<sup>2a</sup>NR<sup>2</sup>-, O, -CR<sup>2</sup>R<sup>2a</sup>O-, and -OCR<sup>2</sup>R<sup>2a</sup>-;

Y is selected from one of the following carbocyclic and heterocyclic systems that are substituted with 0-2 R<sup>4a</sup>;

cyclopropyl, cyclopentyl, cyclohexyl, phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, isoxazolinyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl,

1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl,  
 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl,  
 1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl,  
 benzothiofuranyl, indolyl, benzimidazolyl,  
 5 benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl,  
 benzisothiazolyl, and isoindazolyl;

alternatively, Y is selected from the following bicyclic  
 heteroaryl ring systems:



K is selected from O, S, NH, and N.

15 In another embodiment, the present invention provides a  
 novel compound wherein:

Y is selected from one of the following carbocyclic and  
 heterocyclic systems which are substituted with 0-2 R<sup>4a</sup>;  
 20 phenyl, piperidinyl, piperazinyl, pyridyl,  
 pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl,  
 pyrrolidinyl, oxazolyl, isoxazolyl, thiazolyl,  
 isothiazolyl, pyrazolyl, imidazolyl, oxadiazole,  
 thiadiazole, triazole, 1,2,3-oxadiazole, 1,2,4-  
 25 oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, 1,2,3-  
 thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole,  
 1,3,4-thiadiazole, 1,2,3-triazole, 1,2,4-triazole,  
 1,2,5-triazole, 1,3,4-triazole, benzofuran,  
 benzothiofuran, indole, benzimidazole, benzimidazolone,

benzoxazole, benzthiazole, indazole, benzisoxazole, benzisothiazole, and isoindazole.

5 In another embodiment, the present invention provides a novel compound wherein B is selected from phenyl, pyrrolidino, N-pyrrolidino-carbonyl, morpholino, N-morpholino-carbonyl, 1,2,3-triazolyl, imidazolyl, and benzimidazolyl, and is substituted with 0-1 R<sup>4a</sup>.

10 In another embodiment, the present invention provides a novel compound wherein B is selected from the group: 2-(aminosulfonyl)phenyl, 2-(methylaminosulfonyl)phenyl, 1-pyrrolidinocarbonyl, 2-(methylsulfonyl)phenyl, 2-(N,N-dimethylaminomethyl)phenyl, 2-(N-methylaminomethyl)phenyl, 2-(N-ethyl-N-methylaminomethyl)phenyl, 2-(N-pyrrolidinylmethyl)phenyl, 1-methyl-2-imidazolyl, 2-methyl-1-imidazolyl, 2-(dimethylaminomethyl)-1-imidazolyl, 2-(methylaminomethyl)-1-imidazolyl, 2-(N-(cyclopropylmethyl)aminomethyl)phenyl, 2-(N-(cyclobutyl)aminomethyl)phenyl, 2-(N-(cyclopentyl)aminomethyl)phenyl, 2-(N-(4-hydroxypiperidinyl)methyl)phenyl, and 2-(N-(3-hydroxypyrrolidinyl)methyl)phenyl.

25 In another embodiment, the present invention provides novel pharmaceutical compositions, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of the present invention or a pharmaceutically acceptable salt form thereof.

In another embodiment, the present invention provides a novel method for treating or preventing a thromboembolic disorder, comprising: administering to a patient in need thereof a therapeutically effective amount of a compound of the present invention or a pharmaceutically acceptable salt form thereof.

In another embodiment, the present invention provides a compound of the present invention as described above for use in therapy.

In another embodiment, the present invention provides the use of the present invention as described above for the manufacture of a medicament for the treatment of a thromboembolic disorder.

#### DEFINITIONS

The compounds herein described may have asymmetric centers. Compounds of the present invention containing an asymmetrically substituted atom may be isolated in optically active or racemic forms. It is well known in the art how to prepare optically active forms, such as by resolution of racemic forms or by synthesis from optically active starting materials. Many geometric isomers of olefins, C=N double bonds, and the like can also be present in the compounds described herein, and all such stable isomers are contemplated in the present invention. Cis and trans geometric isomers of the compounds of the present invention are described and may be isolated as a mixture of isomers or as separated isomeric forms. All chiral, diastereomeric, racemic forms and all geometric isomeric forms of a structure are intended, unless the specific stereochemistry or isomeric form is specifically indicated. All processes

used to prepare compounds of the present invention and intermediates made therein are considered to be part of the present invention. All tautomers of shown or described compounds are also considered to be part of the present invention.

The term "substituted," as used herein, means that any one or more hydrogens on the designated atom is replaced with a selection from the indicated group, provided that the designated atom's normal valency is not exceeded, and that the substitution results in a stable compound. When a substituent is keto (i.e., =O), then 2 hydrogens on the atom are replaced. Keto substituents are not present on aromatic moieties.

The present invention is intended to include all isotopes of atoms occurring in the present compounds. Isotopes include those atoms having the same atomic number but different mass numbers. By way of general example and without limitation, isotopes of hydrogen include tritium and deuterium. Isotopes of carbon include C-13 and C-14.

When any variable (e.g.,  $R^6$ ) occurs more than one time in any constituent or formula for a compound, its definition at each occurrence is independent of its definition at every other occurrence. Thus, for example, if a group is shown to be substituted with 0-2  $R^6$ , then said group may optionally be substituted with up to two  $R^6$  groups and  $R^6$  at each occurrence is selected independently from the definition of  $R^6$ . Also, combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

When a bond to a substituent is shown to cross a bond connecting two atoms in a ring, then such substituent may be bonded to any atom on the ring. When a substituent is listed without indicating the atom via which such substituent is bonded to the rest of the compound of a given formula, then such substituent may be bonded via any atom in such

substituent. Combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

As used herein, "alkyl" is intended to include both  
5 branched and straight-chain saturated aliphatic hydrocarbon groups having the specified number of carbon atoms. C<sub>1-10</sub> alkyl, is intended to include C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub>, and C<sub>10</sub> alkyl groups. Examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, and s-pentyl. "Haloalkyl" is  
10 intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups having the specified number of carbon atoms, substituted with 1 or more halogen (for example -C<sub>v</sub>F<sub>w</sub> where v = 1 to 3 and w = 1 to (2v+1)).  
15 Examples of haloalkyl include, but are not limited to, trifluoromethyl, trichloromethyl, pentafluoroethyl, and pentachloroethyl. "Alkoxy" represents an alkyl group as defined above with the indicated number of carbon atoms attached through an oxygen bridge. C<sub>1-10</sub> alkoxy, is intended  
20 to include C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub>, and C<sub>10</sub> alkoxy groups. Examples of alkoxy include, but are not limited to, methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, s-butoxy, t-butoxy, n-pentoxy, and s-pentoxy. "Cycloalkyl" is intended to include saturated ring groups, such as cyclopropyl,  
25 cyclobutyl, or cyclopentyl. C<sub>3-7</sub> cycloalkyl is intended to include C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, and C<sub>7</sub> cycloalkyl groups. "Alkenyl" is intended to include hydrocarbon chains of either straight or branched configuration and one or more unsaturated carbon-carbon bonds that may occur in any stable point along  
30 the chain, such as ethenyl and propenyl. C<sub>2-10</sub> alkenyl is intended to include C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub>, and C<sub>10</sub> alkenyl groups. "Alkynyl" is intended to include hydrocarbon chains of either straight or branched configuration and one or more triple carbon-carbon bonds that may occur in any



stable point along the chain, such as ethynyl and propynyl. C<sub>2-10</sub> Alkynyl is intended to include C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub>, and C<sub>10</sub> alkynyl groups.

"Halo" or "halogen" as used herein refers to fluoro, chloro, bromo, and iodo; and "counterion" is used to represent a small, negatively charged species such as chloride, bromide, hydroxide, acetate, and sulfate.

As used herein, "carbocycle" or "carbocyclic residue" is intended to mean any stable 3, 4, 5, 6, or 7-membered monocyclic or bicyclic or 7, 8, 9, 10, 11, 12, or 13-membered bicyclic or tricyclic, any of which may be saturated, partially unsaturated, or aromatic. Examples of such carbocycles include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, adamantyl, cyclooctyl, [3.3.0]bicyclooctane, [4.3.0]bicyclononane, [4.4.0]bicyclodecane, [2.2.2]bicyclooctane, fluorenyl, phenyl, naphthyl, indanyl, adamantyl, and tetrahydronaphthyl.

As used herein, the term "heterocycle" or "heterocyclic system" is intended to mean a stable 5, 6, or 7-membered monocyclic or bicyclic or 7, 8, 9, or 10-membered bicyclic heterocyclic ring which is saturated, partially unsaturated or unsaturated (aromatic), and which consists of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, NH, O and S and including any bicyclic group in which any of the above-defined heterocyclic rings is fused to a benzene ring. The nitrogen and sulfur heteroatoms may optionally be oxidized. The heterocyclic ring may be attached to its pendant group at any heteroatom or carbon atom that results in a stable structure. The heterocyclic rings described herein may be substituted on carbon or on a nitrogen atom if the resulting compound is stable. A nitrogen in the heterocycle may optionally be quaternized. It is preferred that when the total number of S and O atoms in the heterocycle exceeds 1,

then these heteroatoms are not adjacent to one another. It is preferred that the total number of S and O atoms in the heterocycle is not more than 1. As used herein, the term "aromatic heterocyclic system" or "heteroaryl" is intended to mean a stable 5, 6, or 7-membered monocyclic or bicyclic or 7, 8, 9, or 10-membered bicyclic heterocyclic aromatic ring which consists of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, NH, O and S. It is to be noted that total number of S and O atoms in the aromatic heterocycle is not more than 1.

Examples of heterocycles include, but are not limited to, acridinyl, azocinyl, benzimidazolyl, benzofuranyl, benzothiofuranyl, benzothiophenyl, benzoxazolyl, benzoxazoliny, benzthiazolyl, benztriazolyl, benztetrazolyl, benzisoxazolyl, benzisothiazolyl, benzimidazoliny, carbazolyl, 4aH-carbazolyl, carbolinyl, chromanyl, chromenyl, cinnolinyl, decahydroquinolinyl, 2H,6H-1,5,2-dithiazinyl, dihydrofuro[2,3-b]tetrahydrofuran, furanyl, furazanyl, imidazolidinyl, imidazoliny, imidazolyl, 1H-indazolyl, indolenyl, indolinyl, indoliziny, indolyl, 3H-indolyl, isatinoyl, isobenzofuranyl, isochromanyl, isoindazolyl, isoindolinyl, isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, methylenedioxyphenyl, morpholinyl, naphthyridinyl, octahydroisoquinolinyl, oxadiazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, oxazolidinyl, oxazolyl, oxindolyl, pyrimidinyl, phenanthridinyl, phenanthrolinyl, phenazinyl, phenothiazinyl, phenoxathinyl, phenoxazinyl, phthalazinyl, piperazinyl, piperidinyl, piperidonyl, 4-piperidonyl, piperonyl, pteridinyl, purinyl, pyranyl, pyrazinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl, pyridazinyl, pyridooxazole, pyridoimidazole, pyridothiazole, pyridinyl, pyridyl, pyrimidinyl, pyrrolidinyl, pyrrolinyl, 2H-pyrrolyl, pyrrolyl, quinazolinyl, quinolinyl, 4H-quinoliziny,

quinoxaliny, quinuclidiny, tetrahydrofurany,  
tetrahydroisoquinoliny, tetrahydroquinoliny, tetrazoly,  
6H-1,2,5-thiadiaziny, 1,2,3-thiadiazoly, 1,2,4-  
thiadiazoly, 1,2,5-thiadiazoly, 1,3,4-thiadiazoly,  
5 thianthreny, thiazoly, thieny, thienothiazoly,  
thienooxazoly, thienoimidazoly, thiopheny, triaziny,  
1,2,3-triazoly, 1,2,4-triazoly, 1,2,5-triazoly, 1,3,4-  
triazoly, and xantheny. Also included are fused ring and  
10 spiro compounds containing, for example, the above  
heterocycles.

The phrase "pharmaceutically acceptable" is employed  
herein to refer to those compounds, materials, compositions,  
and/or dosage forms which are, within the scope of sound  
medical judgment, suitable for use in contact with the  
15 tissues of human beings and animals without excessive  
toxicity, irritation, allergic response, or other problem or  
complication, commensurate with a reasonable benefit/risk  
ratio.

As used herein, "pharmaceutically acceptable salts"  
20 refer to derivatives of the disclosed compounds wherein the  
parent compound is modified by making acid or base salts  
thereof. Examples of pharmaceutically acceptable salts  
include, but are not limited to, mineral or organic acid  
salts of basic residues such as amines; alkali or organic  
25 salts of acidic residues such as carboxylic acids; and the  
like. The pharmaceutically acceptable salts include the  
conventional non-toxic salts or the quaternary ammonium  
salts of the parent compound formed, for example, from non-  
toxic inorganic or organic acids. For example, such  
30 conventional non-toxic salts include those derived from  
inorganic acids such as hydrochloric, hydrobromic, sulfuric,  
sulfamic, phosphoric, nitric and the like; and the salts  
prepared from organic acids such as acetic, propionic,  
succinic, glycolic, stearic, lactic, malic, tartaric,  
35 citric, ascorbic, pamoic, maleic, hydroxymaleic,

phenylacetic, glutamic, benzoic, salicylic, sulfanilic, 2-acetoxybenzoic, fumaric, toluenesulfonic, methanesulfonic, ethane disulfonic, oxalic, isethionic, and the like.

5 The pharmaceutically acceptable salts of the present invention can be synthesized from the parent compound that contains a basic or acidic moiety by conventional chemical methods. Generally, such salts can be prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in  
10 water or in an organic solvent, or in a mixture of the two; generally, non-aqueous media like ether, ethyl acetate, ethanol, isopropanol, or acetonitrile are preferred. Lists of suitable salts are found in *Remington's Pharmaceutical Sciences*, 17th ed., Mack Publishing Company, Easton, PA, 1985, p. 1418, the disclosure of which is hereby  
15 incorporated by reference.

Since prodrugs are known to enhance numerous desirable qualities of pharmaceuticals (e.g., solubility, bioavailability, manufacturing, etc...) the compounds of the  
20 present invention may be delivered in prodrug form. Thus, the present invention is intended to cover prodrugs of the presently claimed compounds, methods of delivering the same and compositions containing the same. "Prodrugs" are intended to include any covalently bonded carriers that  
25 release an active parent drug of the present invention *in vivo* when such prodrug is administered to a mammalian subject. Prodrugs the present invention are prepared by modifying functional groups present in the compound in such a way that the modifications are cleaved, either in routine  
30 manipulation or *in vivo*, to the parent compound. Prodrugs include compounds of the present invention wherein a hydroxy, amino, or sulfhydryl group is bonded to any group that, when the prodrug of the present invention is administered to a mammalian subject, it cleaves to form a  
35 free hydroxyl, free amino, or free sulfhydryl group,

respectively. Examples of prodrugs include, but are not limited to, acetate, formate and benzoate derivatives of alcohol and amine functional groups in the compounds of the present invention.

5 "Stable compound" and "stable structure" are meant to indicate a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an efficacious therapeutic agent.

10 "Substituted" is intended to indicate that one or more hydrogens on the atom indicated in the expression using "substituted" is replaced with a selection from the indicated group(s), provided that the indicated atom's normal valency is not exceeded, and that the substitution  
15 results in a stable compound. When a substituent is keto (i.e., =O) group, then 2 hydrogens on the atom are replaced.

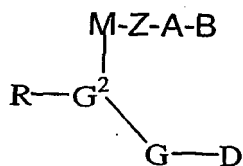
"Therapeutically effective amount" is intended to include an amount of a compound of the present invention or an amount of the combination of compounds claimed effective  
20 to inhibit factor Xa. The combination of compounds is preferably a synergistic combination. Synergy, as described, for example, by Chou and Talalay, *Adv. Enzyme Regul.* **1984**, 22:27-55, occurs when the effect (in this case, inhibition of factor Xa) of the compounds when administered in  
25 combination is greater than the additive effect of the compounds when administered alone as a single agent. In general, a synergistic effect is most clearly demonstrated at sub-optimal concentrations of the compounds. Synergy can be in terms of lower cytotoxicity, increased antiviral  
30 effect, or some other beneficial effect of the combination compared with the individual components.

#### SYNTHESIS

The compounds of the present invention can be prepared  
35 in a number of ways known to one skilled in the art of

organic synthesis. The compounds of the present invention can be synthesized using the methods described below, together with synthetic methods known in the art of synthetic organic chemistry, or by variations thereon as appreciated by those skilled in the art. Preferred methods include, but are not limited to, those described below. The reactions are performed in a solvent appropriate to the reagents and materials employed and suitable for the transformations being effected. It will be understood by those skilled in the art of organic synthesis that the functionality present on the molecule should be consistent with the transformations proposed. This will sometimes require a judgment to modify the order of the synthetic steps or to select one particular process scheme over another in order to obtain a desired compound of the invention. It will also be recognized that another major consideration in the planning of any synthetic route in this field is the judicious choice of the protecting group used for protection of the reactive functional groups present in the compounds described in this invention. An authoritative account describing the many alternatives to the trained practitioner is Greene and Wuts (*Protective Groups In Organic Synthesis*, Wiley and Sons, 1991). All references cited herein are hereby incorporated in their entirety herein by reference.

Scheme 1

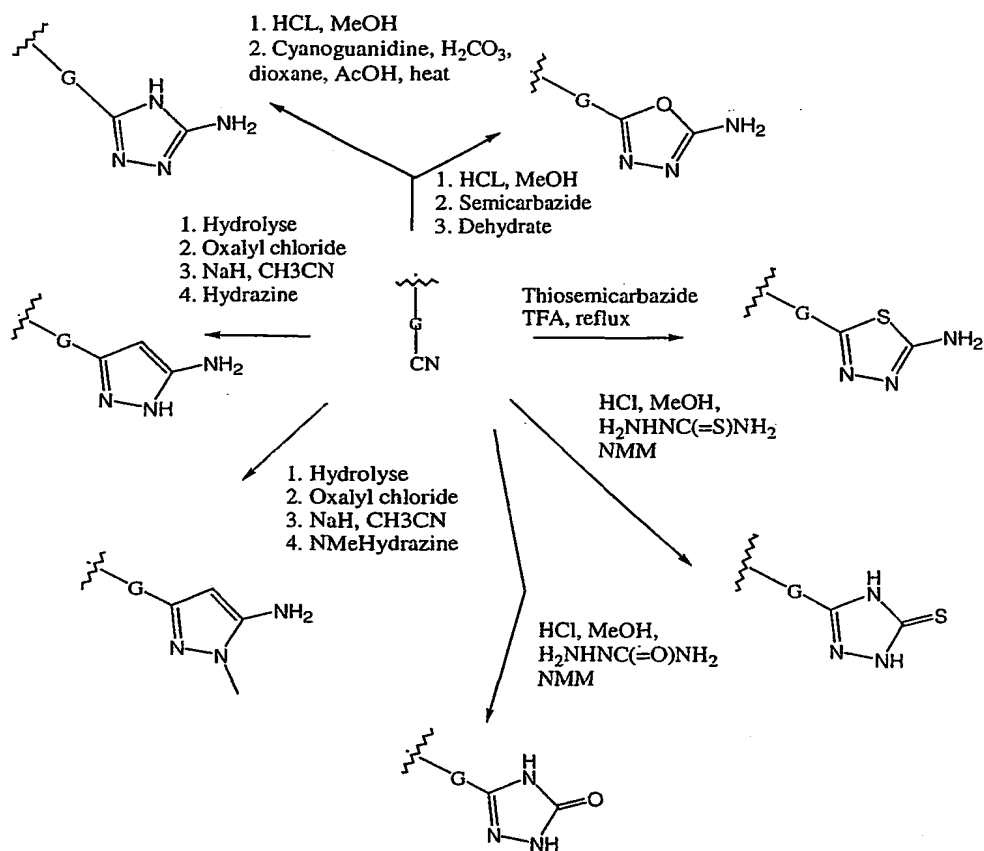


The heterocyclic system shown in Scheme 1 (wherein G-D can be -CN or halo) can be prepared according to the schemes shown in PCT applications WO98/28269, WO98/28282, WO/9857934 and

WO99/32454. In Scheme 1 and the schemes that follow, -G-D represents rings D1, D2, or D3 attached to linker G or precursor to this moiety.

Compounds of this invention wherein G-D is a cyano group can be manipulated to afford thiadiazoles, oxadiazoles, aminooxadiazoles, pyrazoles, triazoles, and triazolones as outlined in Scheme 2.

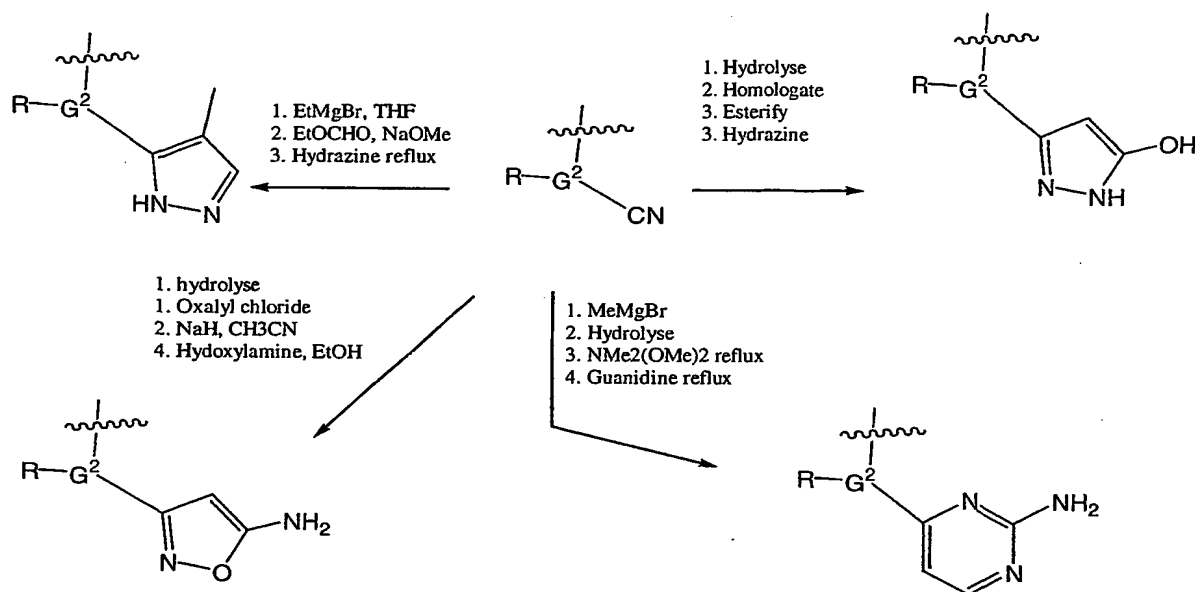
Scheme 2



10

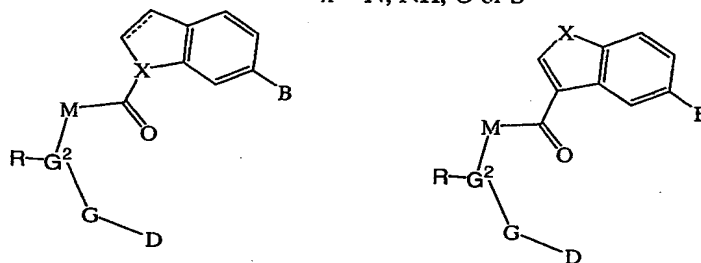
Other heterocycles contained in this invention can also be obtained via methods shown in Scheme 3

## Scheme 3



## Scheme 4

x = N, NH, O or S

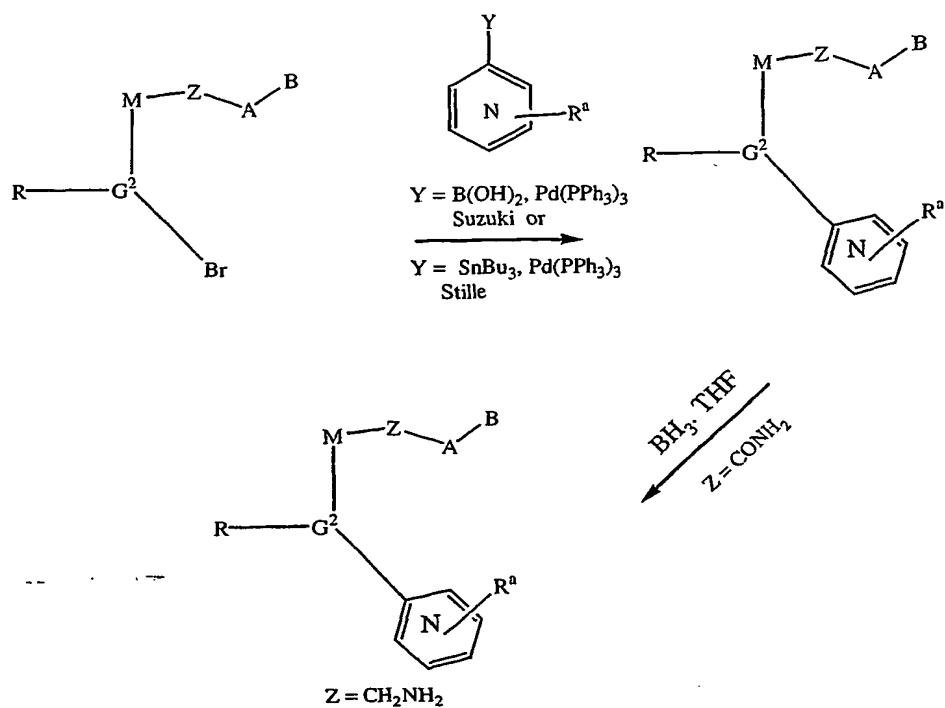


Various analogs of the compounds contained in Scheme 4 can be made following the methodologies outlined in Schemes 1-3 and WO01/05784.

Compounds of this invention wherein ring D is a pyridyl, pyrimidyl, pyridazine, or other heterocyclic ring systems can also be prepared via the Suzuki and or the Stille coupling techniques from easily accessible bromophenyl precursors shown in Scheme 5.

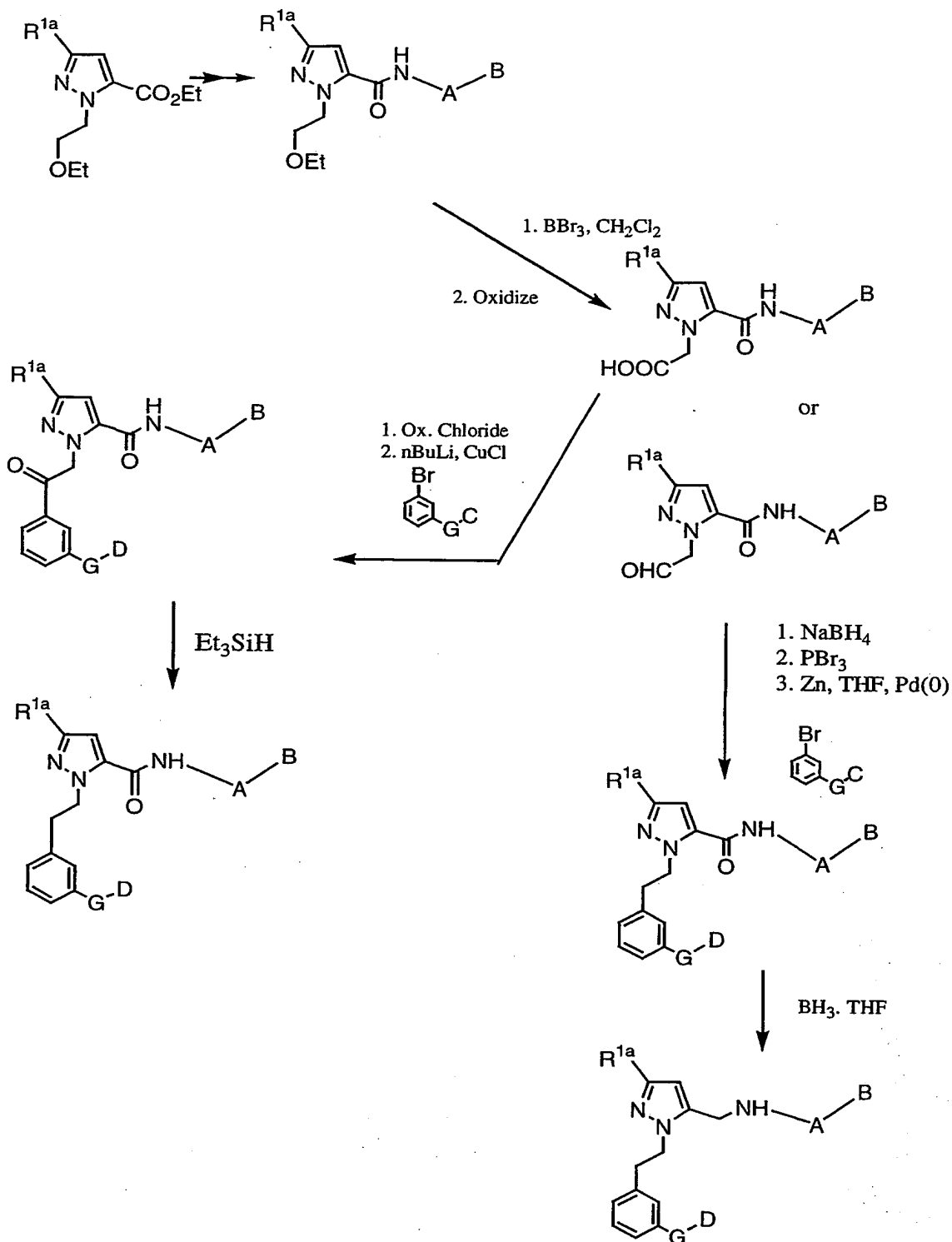


Scheme 5



Additionally, other compounds of this invention can  
 5 also be prepared by those knowledgeable in the art following  
 the methodology outlined in Scheme 6.

Scheme 6

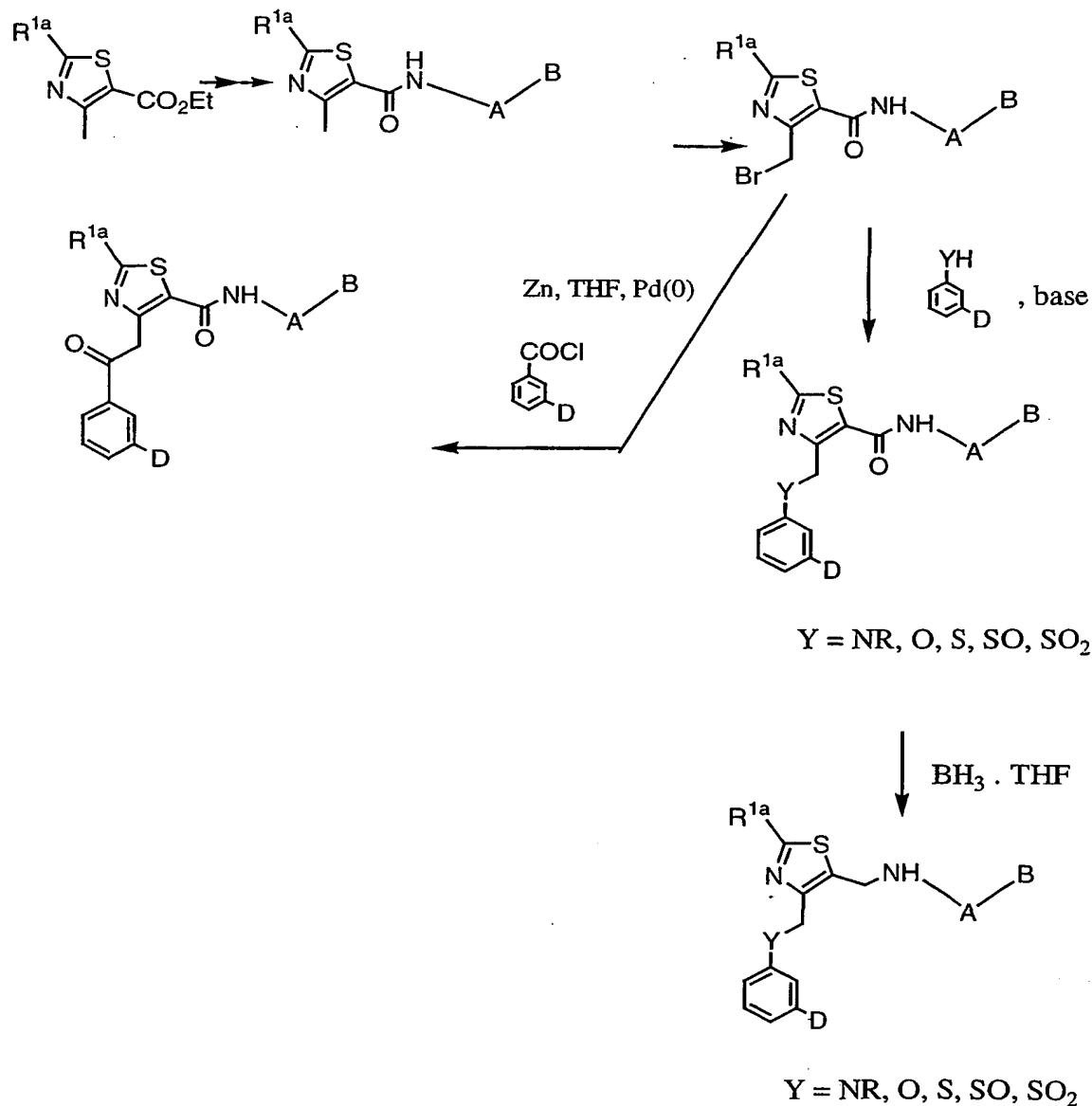


The compounds prepared via Scheme 6 can be used to  
 5 prepare similar analogs with other five membered

heterocyclic core systems or other linker  $G^1$ . These can then be further elaborated via the methodologies shown in earlier schemes to obtain compounds of this invention.

For other carbon based heterocyclic or aryl core systems the above methodologies apply but can be further modified via the method outlined in Scheme 7

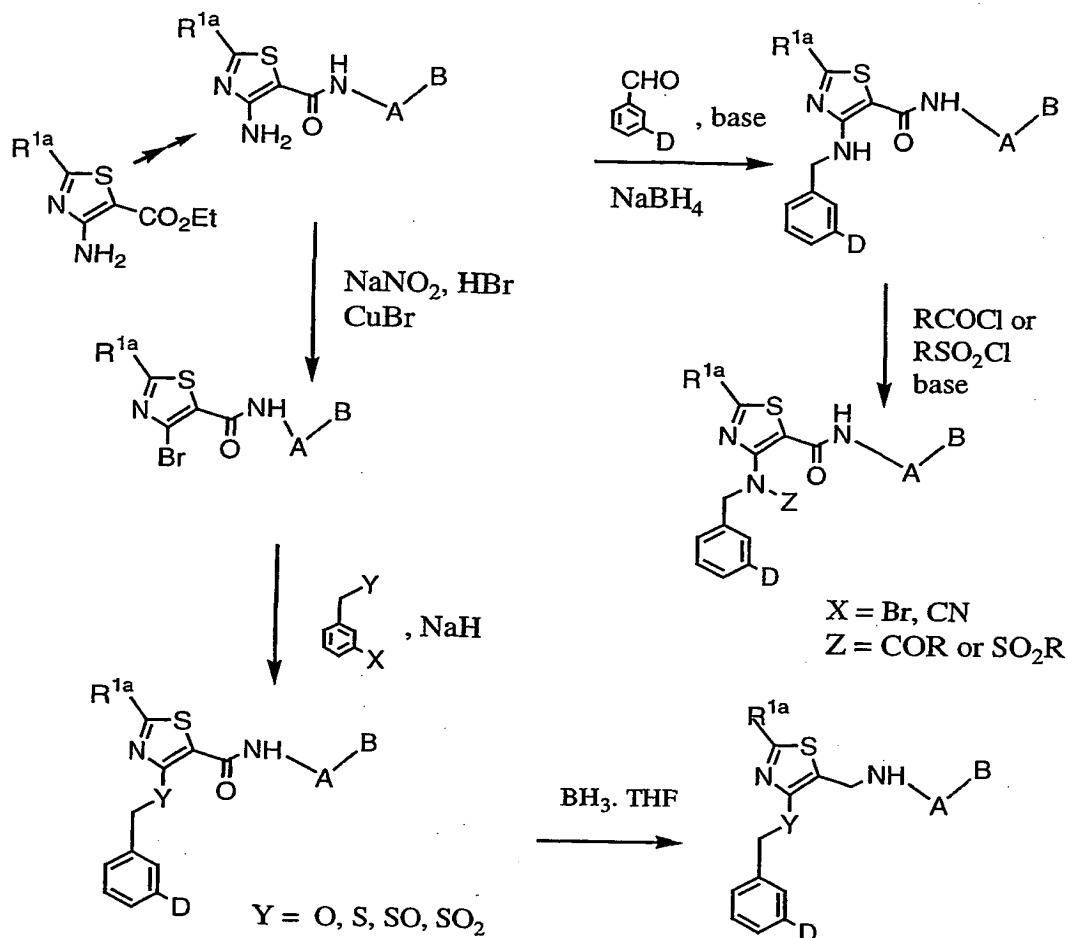
Scheme 7



The synthesis shown in Scheme 7 can be adopted for other carbon based heterocycles or aryl rings. In addition to the above other compounds of this invention can also be prepared via the method outlined in Scheme 8.

5

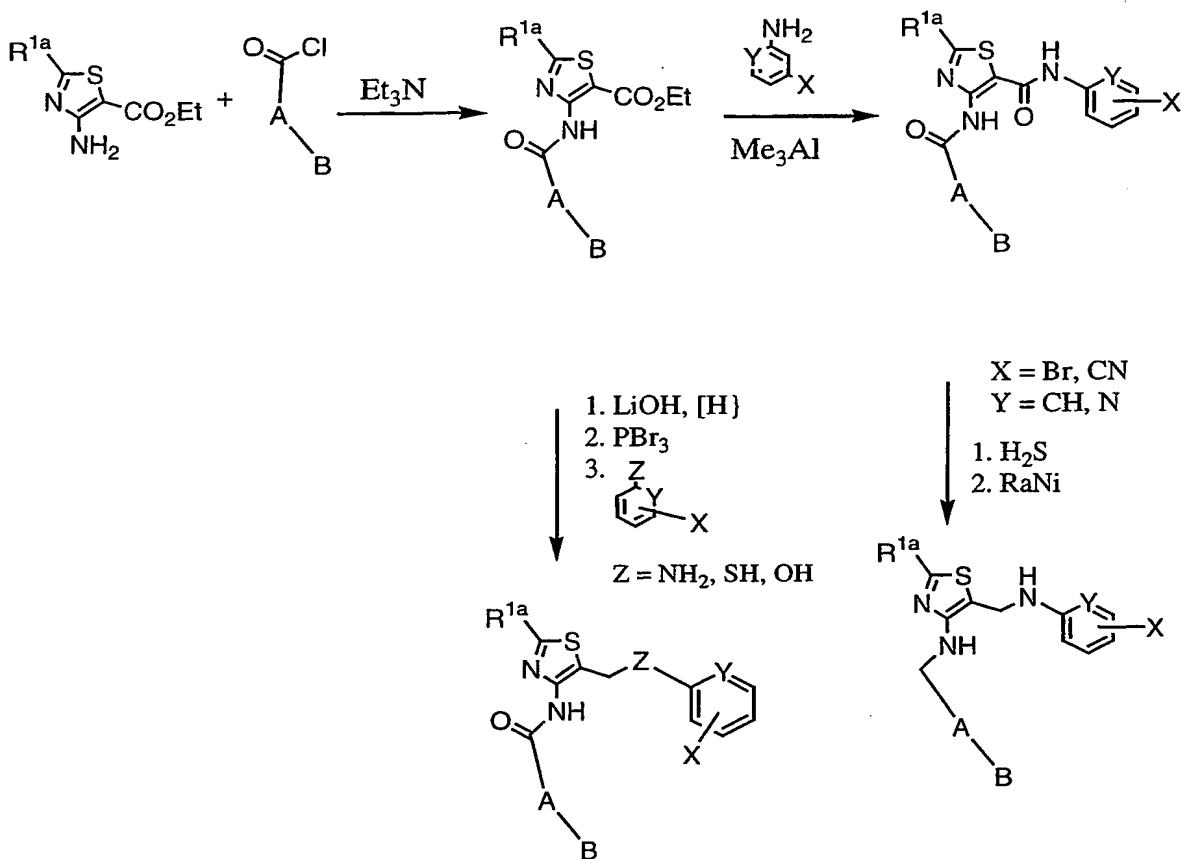
Scheme 8



10

Alternatively, compounds of these inventions can also be prepared via the methodology outlined in Scheme 9.

### Scheme 9



5       The synthetic methodology applied in Scheme 9 can also  
be applied to all other heterocyclic or aryl systems. In  
all the cases and schemes provided the intermediates wherein  
X (or D-G-) is a halogen or cyano group these in turn can be  
manipulated to the heterocyclic systems contained in this  
10 invention.

The compounds of the present invention have a group "A-B" attached to ring M directly or via Z. Preparations of some of the rings M and the "A-B" moieties can follow the same methods described in WO97/23212, WO97/30971, WO97/38984, WO98/01428, WO98/06694, WO98/28269, WO98/28282, WO98/57934, WO98/57937, and WO98/57951, the contents of which are incorporated herein by reference.

## UTILITY

The compounds of this invention are useful as anticoagulants for the treatment or prevention of thromboembolic disorders in mammals. The term "thromboembolic disorders" as used herein includes arterial or venous cardiovascular or cerebrovascular thromboembolic disorders, including, for example, unstable angina, first or recurrent myocardial infarction, ischemic sudden death, transient ischemic attack, stroke, atherosclerosis, venous thrombosis, deep vein thrombosis, thrombophlebitis, arterial embolism, coronary and cerebral arterial thrombosis, cerebral embolism, kidney embolisms, and pulmonary embolisms. The anticoagulant effect of compounds of the present invention is believed to be due to inhibition of factor Xa or thrombin.

The effectiveness of compounds of the present invention as inhibitors of factor Xa was determined using purified human factor Xa and synthetic substrate. The rate of factor Xa hydrolysis of chromogenic substrate S2222 (Kabi Pharmacia, Franklin, OH) was measured both in the absence and presence of compounds of the present invention. Hydrolysis of the substrate resulted in the release of pNA, which was monitored spectrophotometrically by measuring the increase in absorbance at 405 nm. A decrease in the rate of absorbance change at 405 nm in the presence of inhibitor is indicative of enzyme inhibition. The results of this assay are expressed as inhibitory constant,  $K_i$ .

Factor Xa determinations were made in 0.10 M sodium phosphate buffer, pH 7.5, containing 0.20 M NaCl, and 0.5% PEG 8000. The Michaelis constant,  $K_m$ , for substrate hydrolysis was determined at 25°C using the method of Lineweaver and Burk. Values of  $K_i$  were determined by allowing 0.2-0.5 nM human factor Xa (Enzyme Research Laboratories, South Bend, IN) to react with the substrate

(0.20 mM-1 mM) in the presence of inhibitor. Reactions were allowed to go for 30 minutes and the velocities (rate of absorbance change vs time) were measured in the time frame of 25-30 minutes. The following relationship was used to

5 calculate  $K_i$  values:

$$(v_o - v_s) / v_s = I / (K_i (1 + S / K_m))$$

where:

$v_o$  is the velocity of the control in the absence of inhibitor;

10  $v_s$  is the velocity in the presence of inhibitor;

$I$  is the concentration of inhibitor;

$K_i$  is the dissociation constant of the enzyme:inhibitor complex;

$S$  is the concentration of substrate;

15  $K_m$  is the Michaelis constant.

Using the methodology described above, some compounds of the present invention were found to exhibit a  $K_i$  of  $\leq 10 \mu\text{M}$ , thereby confirming the utility of the compounds of the present invention as effective Xa inhibitors.

20 Compounds tested in the above assay are considered to be active if they exhibit a  $K_i$  of  $\leq 10 \mu\text{M}$ . Preferred compounds of the present invention have  $K_i$ 's of  $\leq 1 \mu\text{M}$ . More preferred compounds of the present invention have  $K_i$ 's of  $\leq 0.1 \mu\text{M}$ . Even more preferred compounds of the present invention have  $K_i$ 's of  $\leq 0.01 \mu\text{M}$ . Still more preferred compounds of the present invention have  $K_i$ 's of  $\leq 0.001 \mu\text{M}$ .

The antithrombotic effect of compounds of the present invention can be demonstrated in a rabbit arterio-venous (AV) shunt thrombosis model. In this model, rabbits weighing 30 2-3 kg anesthetized with a mixture of xylazine (10 mg/kg i.m.) and ketamine (50 mg/kg i.m.) are used. A saline-filled AV shunt device is connected between the femoral arterial and the femoral venous cannulae. The AV shunt device consists of a piece of 6-cm tygon tubing that contains a

piece of silk thread. Blood will flow from the femoral artery via the AV-shunt into the femoral vein. The exposure of flowing blood to a silk thread will induce the formation of a significant thrombus. After forty minutes, the shunt is  
5 disconnected and the silk thread covered with thrombus is weighed. Test agents or vehicle will be given (i.v., i.p., s.c., or orally) prior to the opening of the AV shunt. The percentage inhibition of thrombus formation is determined for each treatment group. The ID50 values (dose which  
10 produces 50% inhibition of thrombus formation) are estimated by linear regression.

The compounds of the present invention may also be useful as inhibitors of serine proteases, notably human thrombin, plasma kallikrein and plasmin. Because of their  
15 inhibitory action, these compounds are indicated for use in the prevention or treatment of physiological reactions, blood coagulation and inflammation, catalyzed by the aforesaid class of enzymes. Specifically, the compounds have utility as drugs for the treatment of diseases arising from  
20 elevated thrombin activity such as myocardial infarction, and as reagents used as anticoagulants in the processing of blood to plasma for diagnostic and other commercial purposes.

Some compounds of the present invention were shown to  
25 be direct acting inhibitors of the serine protease thrombin by their ability to inhibit the cleavage of small molecule substrates by thrombin in a purified system. *In vitro* inhibition constants were determined by the method described by Kettner et al. in *J. Biol. Chem.* **1990**, 265, 18289-18297,  
30 herein incorporated by reference. In these assays, thrombin-mediated hydrolysis of the chromogenic substrate S2238 (Helena Laboratories, Beaumont, TX) was monitored spectrophotometrically. Addition of an inhibitor to the assay mixture results in decreased absorbance and is  
35 indicative of thrombin inhibition. Human thrombin (Enzyme



Research Laboratories, Inc., South Bend, IN) at a concentration of 0.2 nM in 0.10 M sodium phosphate buffer, pH 7.5, 0.20 M NaCl, and 0.5% PEG 6000, was incubated with various substrate concentrations ranging from 0.20 to 0.02 mM. After 25 to 30 minutes of incubation, thrombin activity was assayed by monitoring the rate of increase in absorbance at 405 nm that arises owing to substrate hydrolysis.

Inhibition constants were derived from reciprocal plots of the reaction velocity as a function of substrate

concentration using the standard method of Lineweaver and Burk. Using the methodology described above, some compounds of this invention were evaluated and found to exhibit a  $K_i$  of less than 10  $\mu\text{M}$ , thereby confirming the utility of the compounds of the present invention as effective thrombin inhibitors.

The compounds of the present invention can be administered alone or in combination with one or more additional therapeutic agents. These include other anti-coagulant or coagulation inhibitory agents, anti-platelet or platelet inhibitory agents, thrombin inhibitors, or thrombolytic or fibrinolytic agents.

The compounds are administered to a mammal in a therapeutically effective amount. By "therapeutically effective amount" it is meant an amount of a compound of the present invention that, when administered alone or in combination with an additional therapeutic agent to a mammal, is effective to prevent or ameliorate the thromboembolic disease condition or the progression of the disease.

By "administered in combination" or "combination therapy" it is meant that the compound of the present invention and one or more additional therapeutic agents are administered concurrently to the mammal being treated. When administered in combination each component may be administered at the same time or sequentially in any order

at different points in time. Thus, each component may be administered separately but sufficiently closely in time so as to provide the desired therapeutic effect. Other anticoagulant agents (or coagulation inhibitory agents) that  
5 may be used in combination with the compounds of this invention include warfarin and heparin, as well as other factor Xa inhibitors such as those described in the publications identified above under Background of the Invention.

10 The term anti-platelet agents (or platelet inhibitory agents), as used herein, denotes agents that inhibit platelet function such as by inhibiting the aggregation, adhesion or granular secretion of platelets. Such agents include, but are not limited to, the various known  
15 non-steroidal anti-inflammatory drugs (NSAIDS) such as aspirin, ibuprofen, naproxen, sulindac, indomethacin, mefenamate, droxicam, diclofenac, sulfinpyrazone, and piroxicam, including pharmaceutically acceptable salts or prodrugs thereof. Of the NSAIDS, aspirin (acetylsalicyclic acid or ASA), and piroxicam are preferred. Other suitable  
20 anti-platelet agents include ticlopidine, including pharmaceutically acceptable salts or prodrugs thereof. Ticlopidine is also a preferred compound since it is known to be gentle on the gastro-intestinal tract in use. Still  
25 other suitable platelet inhibitory agents include IIb/IIIa antagonists, thromboxane-A2-receptor antagonists and thromboxane-A2-synthetase inhibitors, as well as pharmaceutically acceptable salts or prodrugs thereof.

The term thrombin inhibitors (or anti-thrombin agents),  
30 as used herein, denotes inhibitors of the serine protease thrombin. By inhibiting thrombin, various thrombin-mediated processes, such as thrombin-mediated platelet activation (that is, for example, the aggregation of platelets, and/or the granular secretion of plasminogen activator inhibitor-1  
35 and/or serotonin) and/or fibrin formation are disrupted. A

number of thrombin inhibitors are known to one of skill in the art and these inhibitors are contemplated to be used in combination with the present compounds. Such inhibitors include, but are not limited to, boroarginine derivatives, boroptides, heparins, hirudin and argatroban, including pharmaceutically acceptable salts and prodrugs thereof. Boroarginine derivatives and boroptides include N-acetyl and peptide derivatives of boronic acid, such as C-terminal a-aminoboronic acid derivatives of lysine, ornithine, arginine, homoarginine and corresponding isothiuronium analogs thereof. The term hirudin, as used herein, includes suitable derivatives or analogs of hirudin, referred to herein as hirulogs, such as disulfatohirudin. Boroptide thrombin inhibitors include compounds described in Kettner et al., U.S. Patent No. 5,187,157 and European Patent Application Publication Number 293 881 A2, the disclosures of which are hereby incorporated herein by reference. Other suitable boroarginine derivatives and boroptide thrombin inhibitors include those disclosed in PCT Application Publication Number 92/07869 and European Patent Application Publication Number 471,651 A2, the disclosures of which are hereby incorporated herein by reference.

The term thrombolytics (or fibrinolytic) agents (or thrombolytics or fibrinolytics), as used herein, denotes agents that lyse blood clots (thrombi). Such agents include tissue plasminogen activator, anistreplase, urokinase or streptokinase, including pharmaceutically acceptable salts or prodrugs thereof. The term anistreplase, as used herein, refers to anisoylated plasminogen streptokinase activator complex, as described, for example, in European Patent Application No. 028,489, the disclosure of which is hereby incorporated herein by reference herein. The term urokinase, as used herein, is intended to denote both dual and single chain urokinase, the latter also being referred to herein as prourokinase.

Administration of the compounds of the present invention in combination with such additional therapeutic agent, may afford an efficacy advantage over the compounds and agents alone, and may do so while permitting the use of lower doses of each. A lower dosage minimizes the potential of side effects, thereby providing an increased margin of safety.

The compounds of the present invention are also useful as standard or reference compounds, for example as a quality standard or control, in tests or assays involving the inhibition of factor Xa. Such compounds may be provided in a commercial kit, for example, for use in pharmaceutical research involving factor Xa. For example, a compound of the present invention could be used as a reference in an assay to compare its known activity to a compound with an unknown activity. This would ensure the experimenter that the assay was being performed properly and provide a basis for comparison, especially if the test compound was a derivative of the reference compound. When developing new assays or protocols, compounds according to the present invention could be used to test their effectiveness.

The compounds of the present invention may also be used in diagnostic assays involving factor Xa. For example, the presence of factor Xa in an unknown sample could be determined by addition of chromogenic substrate S2222 to a series of solutions containing test sample and optionally one of the compounds of the present invention. If production of pNA is observed in the solutions containing test sample, but not in the presence of a compound of the present invention, then one would conclude factor Xa was present.

#### Dosage and Formulation

The compounds of this invention can be administered in such oral dosage forms as tablets, capsules (each of which includes sustained release or timed release

formulations), pills, powders, granules, elixirs, tinctures, suspensions, syrups, and emulsions. They may also be administered in intravenous (bolus or infusion), intraperitoneal, subcutaneous, or intramuscular form, all using dosage forms well known to those of ordinary skill in the pharmaceutical arts. They can be administered alone, but generally will be administered with a pharmaceutical carrier selected on the basis of the chosen route of administration and standard pharmaceutical practice.

The dosage regimen for the compounds of the present invention will, of course, vary depending upon known factors, such as the pharmacodynamic characteristics of the particular agent and its mode and route of administration; the species, age, sex, health, medical condition, and weight of the recipient; the nature and extent of the symptoms; the kind of concurrent treatment; the frequency of treatment; the route of administration, the renal and hepatic function of the patient, and the effect desired. A physician or veterinarian can determine and prescribe the effective amount of the drug required to prevent, counter, or arrest the progress of the thromboembolic disorder.

By way of general guidance, the daily oral dosage of each active ingredient, when used for the indicated effects, will range between about 0.001 to 1000 mg/kg of body weight, preferably between about 0.01 to 100 mg/kg of body weight per day, and most preferably between about 1.0 to 20 mg/kg/day. Intravenously, the most preferred doses will range from about 1 to about 10 mg/kg/minute during a constant rate infusion. Compounds of this invention may be administered in a single daily dose, or the total daily dosage may be administered in divided doses of two, three, or four times daily.

Compounds of this invention can be administered in intranasal form via topical use of suitable intranasal vehicles, or via transdermal routes, using transdermal skin

patches. When administered in the form of a transdermal delivery system, the dosage administration will, of course, be continuous rather than intermittent throughout the dosage regimen.

5       The compounds are typically administered in admixture with suitable pharmaceutical diluents, excipients, or carriers (collectively referred to herein as pharmaceutical carriers) suitably selected with respect to the intended form of administration, that is, oral tablets, capsules,  
10       elixirs, syrups and the like, and consistent with conventional pharmaceutical practices.

For instance, for oral administration in the form of a tablet or capsule, the active drug component can be combined with an oral, non-toxic, pharmaceutically acceptable, inert  
15       carrier such as lactose, starch, sucrose, glucose, methyl cellulose, magnesium stearate, dicalcium phosphate, calcium sulfate, mannitol, sorbitol and the like; for oral administration in liquid form, the oral drug components can be combined with any oral, non-toxic, pharmaceutically  
20       acceptable inert carrier such as ethanol, glycerol, water, and the like. Moreover, when desired or necessary, suitable binders, lubricants, disintegrating agents, and coloring agents can also be incorporated into the mixture. Suitable binders include starch, gelatin, natural sugars such as  
25       glucose or beta-lactose, corn sweeteners, natural and synthetic gums such as acacia, tragacanth, or sodium alginate, carboxymethylcellulose, polyethylene glycol, waxes, and the like. Lubricants used in these dosage forms include sodium oleate, sodium stearate, magnesium stearate,  
30       sodium benzoate, sodium acetate, sodium chloride, and the like. Disintegrators include, without limitation, starch, methyl cellulose, agar, bentonite, xanthan gum, and the like.

The compounds of the present invention can also be  
35       administered in the form of liposome delivery systems, such

as small unilamellar vesicles, large unilamellar vesicles, and multilamellar vesicles. Liposomes can be formed from a variety of phospholipids, such as cholesterol, stearylamine, or phosphatidylcholines.

5       Compounds of the present invention may also be coupled with soluble polymers as targetable drug carriers. Such polymers can include polyvinylpyrrolidone, pyran copolymer, polyhydroxypropylmethacrylamide-phenol, polyhydroxyethylaspartamidephenol, or polyethyleneoxide-  
10 polylysine substituted with palmitoyl residues. Furthermore, the compounds of the present invention may be coupled to a class of biodegradable polymers useful in achieving controlled release of a drug, for example, polylactic acid, polyglycolic acid, copolymers of polylactic and polyglycolic  
15 acid, polyepsilon caprolactone, polyhydroxy butyric acid, polyorthoesters, polyacetals, polydihydropyrans, polycyanoacylates, and crosslinked or amphipathic block copolymers of hydrogels.

Dosage forms (pharmaceutical compositions) suitable for  
20 administration may contain from about 1 milligram to about 100 milligrams of active ingredient per dosage unit. In these pharmaceutical compositions the active ingredient will ordinarily be present in an amount of about 0.5-95% by weight based on the total weight of the composition.

25       Gelatin capsules may contain the active ingredient and powdered carriers, such as lactose, starch, cellulose derivatives, magnesium stearate, stearic acid, and the like. Similar diluents can be used to make compressed tablets. Both tablets and capsules can be manufactured as sustained  
30 release products to provide for continuous release of medication over a period of hours. Compressed tablets can be sugar coated or film coated to mask any unpleasant taste and protect the tablet from the atmosphere, or enteric coated for selective disintegration in the gastrointestinal tract.

Liquid dosage forms for oral administration can contain coloring and flavoring to increase patient acceptance.

In general, water, a suitable oil, saline, aqueous dextrose (glucose), and related sugar solutions and glycols  
5 such as propylene glycol or polyethylene glycols are suitable carriers for parenteral solutions. Solutions for parenteral administration preferably contain a water soluble salt of the active ingredient, suitable stabilizing agents, and if necessary, buffer substances. Antioxidizing agents  
10 such as sodium bisulfite, sodium sulfite, or ascorbic acid, either alone or combined, are suitable stabilizing agents. Also used are citric acid and its salts and sodium EDTA. In addition, parenteral solutions can contain preservatives, such as benzalkonium chloride, methyl- or propyl-paraben,  
15 and chlorobutanol.

Suitable pharmaceutical carriers are described in Remington's Pharmaceutical Sciences, Mack Publishing Company, a standard reference text in this field.

Representative useful pharmaceutical dosage-forms for  
20 administration of the compounds of this invention can be illustrated as follows:

#### Capsules

A large number of unit capsules can be prepared by filling standard two-piece hard gelatin capsules each with  
25 100 milligrams of powdered active ingredient, 150 milligrams of lactose, 50 milligrams of cellulose, and 6 milligrams magnesium stearate.

#### Soft Gelatin Capsules

A mixture of active ingredient in a digestable oil  
30 such as soybean oil, cottonseed oil or olive oil may be prepared and injected by means of a positive displacement pump into gelatin to form soft gelatin capsules containing 100 milligrams of the active ingredient. The capsules should be washed and dried.



### Tablets

Tablets may be prepared by conventional procedures so that the dosage unit is 100 milligrams of active ingredient, 0.2 milligrams of colloidal silicon dioxide, 5 milligrams of magnesium stearate, 275 milligrams of microcrystalline cellulose, 11 milligrams of starch and 98.8 milligrams of lactose. Appropriate coatings may be applied to increase palatability or delay absorption.

### Injectable

A parenteral composition suitable for administration by injection may be prepared by stirring 1.5% by weight of active ingredient in 10% by volume propylene glycol and water. The solution should be made isotonic with sodium chloride and sterilized.

### Suspension

An aqueous suspension can be prepared for oral administration so that each 5 mL contain 100 mg of finely divided active ingredient, 200 mg of sodium carboxymethyl cellulose, 5 mg of sodium benzoate, 1.0 g of sorbitol solution, U.S.P., and 0.025 mL of vanillin.

Where the compounds of this invention are combined with other anticoagulant agents, for example, a daily dosage may be about 0.1 to 100 milligrams of the compound of the present invention and about 1 to 7.5 milligrams of the second anticoagulant, per kilogram of patient body weight. For a tablet dosage form, the compounds of this invention generally may be present in an amount of about 5 to 10 milligrams per dosage unit, and the second anti-coagulant in an amount of about 1 to 5 milligrams per dosage unit.

Where the compounds of the present invention are administered in combination with an anti-platelet agent, by way of general guidance, typically a daily dosage may be about 0.01 to 25 milligrams of the compound of the present invention and about 50 to 150 milligrams of the anti-platelet agent, preferably about 0.1 to 1 milligrams of the

compound of the present invention and about 1 to 3 milligrams of anti-platelet agents, per kilogram of patient body weight.

Where the compounds of the present invention are  
5 administered in combination with thrombolytic agent,  
typically a daily dosage may be about 0.1 to 1 milligrams of  
the compound of the present invention, per kilogram of  
patient body weight and, in the case of the thrombolytic  
agents, the usual dosage of the thrombolytic agent when  
10 administered alone may be reduced by about 70-80% when  
administered with a compound of the present invention.

Where two or more of the foregoing second therapeutic  
agents are administered with the compound of the present  
invention, generally the amount of each component in a  
15 typical daily dosage and typical dosage form may be reduced  
relative to the usual dosage of the agent when administered  
alone, in view of the additive or synergistic effect of the  
therapeutic agents when administered in combination.

Particularly when provided as a single dosage unit, the  
20 potential exists for a chemical interaction between the  
combined active ingredients. For this reason, when the  
compound of the present invention and a second therapeutic  
agent are combined in a single dosage unit they are  
formulated such that although the active ingredients are  
25 combined in a single dosage unit, the physical contact  
between the active ingredients is minimized (that is,  
reduced). For example, one active ingredient may be enteric  
coated. By enteric coating one of the active ingredients, it  
is possible not only to minimize the contact between the  
30 combined active ingredients, but also, it is possible to  
control the release of one of these components in the  
gastrointestinal tract such that one of these components is  
not released in the stomach but rather is released in the  
intestines. One of the active ingredients may also be coated  
35 with a material that effects a sustained-release throughout

the gastrointestinal tract and also serves to minimize physical contact between the combined active ingredients.

Furthermore, the sustained-released component can be additionally enteric coated such that the release of this

5 component occurs only in the intestine. Still another approach would involve the formulation of a combination product in which the one component is coated with a sustained and/or enteric release polymer, and the other component is also coated with a polymer such as a low-

10 viscosity grade of hydroxypropyl methylcellulose (HPMC) or other appropriate materials as known in the art, in order to further separate the active components. The polymer coating serves to form an additional barrier to interaction with the other component.

15 These as well as other ways of minimizing contact between the components of combination products of the present invention, whether administered in a single dosage form or administered in separate forms but at the same time by the same manner, will be readily apparent to those skilled in  
20 the art, once armed with the present disclosure.

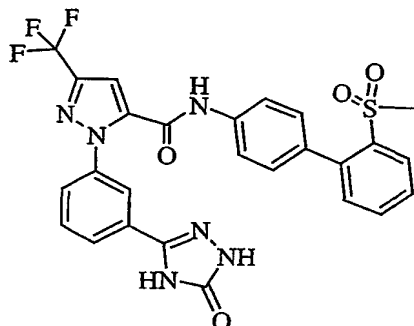
Other features of the invention will become apparent in the course of the following descriptions of exemplary embodiments that are given for illustration of the invention and are not intended to be limiting thereof.

25

## EXAMPLES

## Example 1

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-5-[(2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole



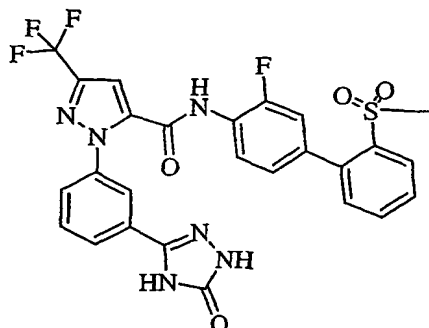
Part A: The starting nitrile, 1-(3-cyanophenyl)-3-trifluoromethyl-5-[(2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole, was prepared according to the methodology described in WO98/28269 (see Example 73). To 0.54 g (1.06 mmol) of this nitrile in anhydrous ethanol was bubbled HCl gas for 0.5h. The reaction mixture was capped and allowed to stir at room temperature for 18h. The ethanol was evaporated to afford the crude ethoxyimide intermediate. LRMS (NH<sub>3</sub>-CI) m/z (relative intensity) 557 (M=H, 100).

Part B: To the crude product in dioxane (10 mL) from part A was added N-Methyl morpholine (0.6 mL, 5.03 mmol). To this mixture was added semicarbazide hydrochloride (0.13 g, 1.06 mmol) and the reaction mixture was refluxed gently for 72h. The mixture was cooled, poured in water (100 mL) and the organics were extracted with ethyl acetate (2x50 mL), dried and evaporated to a brown mass. The crude mixture was purified via reverse-phase HPLC to afford the title compound. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 300MHz) δ: 12.91 (s, 1H), 11.81 (s, 1H), 10.90 (s, 1H), 8.08 (d, 1H, J=7.7Hz), 7.98 (s, 1H), 7.92-7.90 (m, 1H), 7.78-7.64 (m, 7H), 7.41-7.38 (m, 3H),

2.84 (s, 3H) ppm. LRMS (ES+): m/z 591 (M+Na). HRMS (ESI):  
for C<sub>26</sub>H<sub>20</sub>SF<sub>3</sub>O<sub>4</sub>N<sub>6</sub> Mass= 569.1206.

### Example 2

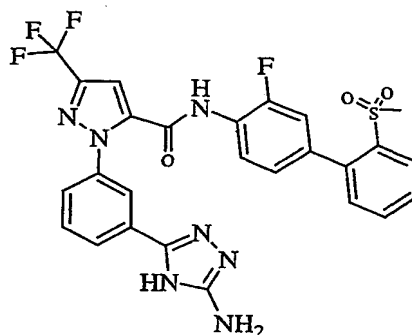
5        1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-  
trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-  
biphen-4-yl)aminocarbonyl]pyrazole



10        The starting nitrile, 1-(3-cyanophenyl)-3-  
trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-  
biphen-4-yl)aminocarbonyl]pyrazole, was prepared according  
to the methodology described in WO98/28269 (see Example  
206). The title compound was prepared from this nitrile in a  
similar method to that described for Example 1. <sup>1</sup>HNMR (DMSO-  
15        d<sub>6</sub>, 300MHz) δ: 12.17 (s, 1H), 11.81 (s, 1H), 10.73 (s, 1H),  
8.09 (dd, 1H, J<sub>1</sub>=J<sub>2</sub>=8.0Hz), 7.99 (s, 1H), 7.93-7.90 (m, 1H),  
7.81-7.64 (m, 6H), 7.43 (dd, 1H, J<sub>1</sub>=J<sub>2</sub>=7.0Hz), 7.38 (dd, 1H,  
J<sub>1</sub>=J<sub>2</sub>=11.0Hz), 7.24 (d, 1H, J=8.0Hz), 2.92 (s, 3H) ppm. LRMS  
(ES+): m/z 587 (M+H) 609 (M+Na). HRMS (ESI): for C<sub>26</sub>H<sub>19</sub>SF<sub>4</sub>O<sub>4</sub>N<sub>6</sub>  
20        Mass= 587.1123.

## Example 3

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole trifluoroacetic acid salt



5

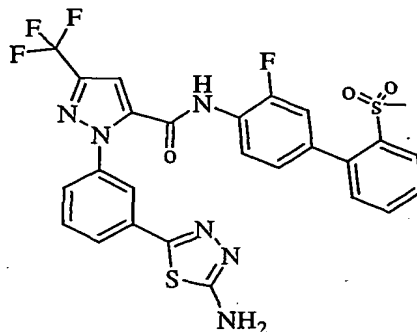
Part A: The nitrile employed for Example 2 was utilized for the preparation of Example 3. Hydrogen chloride was bubbled into an ice-cooled solution of the nitrile (0.52 g, 0.98 mmol) in anhydrous ethanol (50 mL) for 0.5h. The reaction mixture was allowed to warm to ambient temperature overnight and then concentrated *in vacuo*. The crude ethyl imidate hydrochloride was placed under high vacuum and used directly in the next step.

Part B: Acetic acid (1.0 mL) was added to a suspension of crude imidate hydrochloride (0.98 mmol) obtained in part A and aminoguanidine bicarbonate (0.18 g, 1.31 mmol) in 1,4-dioxane (25 mL). The reaction mixture was refluxed for 48h and then concentrated under reduced pressure. The crude solid was purified by reverse phase HPLC. <sup>1</sup>HNMR (DMSO-d<sub>6</sub>, 300MHz) δ: 10.74 (s, 1H), 8.88-7.99 (m, 3H), 7.80-7.69 (m, 4H), 7.62-7.60 (m, 2H), 7.44-7.36 (m, 2H), 7.24-7.22 (m, 1H), 2.92 (s, 3H) ppm. LRMS (ES<sup>+</sup>): m/z 586 (M+H) 608 (M+Na). HRMS (ESI): for C<sub>26</sub>H<sub>20</sub>SF<sub>4</sub>O<sub>3</sub>N<sub>6</sub> Mass= 586.1280.

25

**Example 4**

**1-[3-(2'-Amino-3',4'-thiadiazol-5'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole trifluoroacetic acid salt**



5

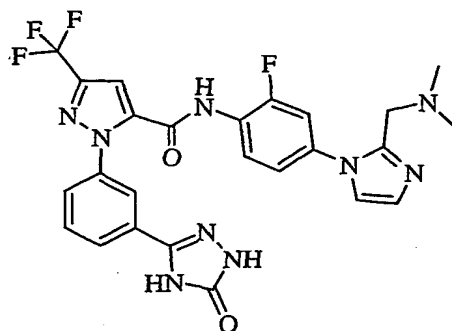
The nitrile employed for Example 2 was dissolved in TFA (2 mL). To this mixture was added thiosemicarbazide (0.13 g, 1.42 mmol) and the reaction mixture was gently refluxed for 2h. The reaction was then concentrated and the crude oil was purified via reverse phase HPLC to afford the title compound. <sup>1</sup>HNMR (DMSO-d<sub>6</sub>, 300MHz) δ: 10.73 (s, 1H), 8.10 (d, 1H, J=8.0Hz), 7.95 (s, 1H), 7.87-7.86 (m, 1H), 7.80-7.62 (m, 8H), 7.44 (d, 1H, J=8.0Hz), 7.38 (d, 1H, J=11.0Hz), 7.24 (d, 1H, J=8.0Hz), 2.92 (s, 3H) ppm. LRMS (ES<sup>+</sup>): m/z 625 (M+Na). HRMS (ESI): for C<sub>26</sub>H<sub>19</sub>S<sub>2</sub>F<sub>4</sub>O<sub>3</sub>N<sub>6</sub> Mass= 603.0889.

15

**Example 5**

**1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-5-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl]aminocarbonyl]pyrazole trifluoroacetic acid salt**

20

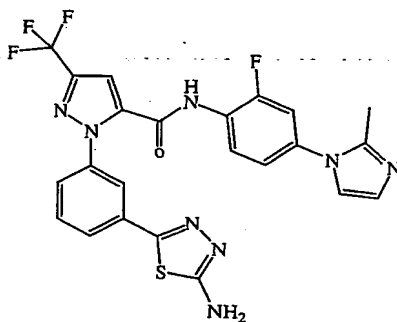


Part A: 1-(3-Cyanophenyl)-3-trifluoromethylpyrazole-5-carboxylic acid was prepared according the methods of WO98/28269 (see Example 14). The pyrazole acid chloride (2.48 mmol) was coupled with 2-fluoro-N,N-dimethyl-2-aminomethyl-4-imidazoloaniline (1.04 g, 2.25 mmol) using DMAP (1.38 g, 11.26 mmol) in dichloromethane. After 48h the reaction mixture was concentrated, dissolved in EtOAc, and washed three times with brine. Then the organics were dried over MgSO<sub>4</sub> and concentrated under reduced pressure. The crude material was purified by flash chromatography. <sup>1</sup>HNMR (DMSO-d<sub>6</sub>, 300MHz) δ: 10.72 (s, 1H), 8.16 (s, 1H), 8.01 (d, 1H, J=8Hz), 7.93 (d, 1H, J=8Hz), 7.77-7.69 (m, 4H), 7.51-7.47 (m, 2H), 7.00 (s, 1H), 3.38 (s, 2H), 2.13 (s, 6H) ppm; LRMS: m/z 496 (M-H).

Part B: The coupling product was converted to its corresponding methylimidate via the Pinner reaction. The imidate (1.62 mmol) was then treated with semicarbazide (0.22 g, 1.94 mmol) in refluxing 1,4-dioxane (40 mL) for 48h. The reaction mixture was concentrated to give the crude aminooxadiazole. The product was purified by HPLC. LRMS: m/z 556 (M+H).

#### Example 6

1-[3-(2'-Amino-3',4'-thiadiazol-5'-yl)phenyl]-3-trifluoromethyl-5-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl]aminocarbonylpyrazole trifluoroacetic acid salt



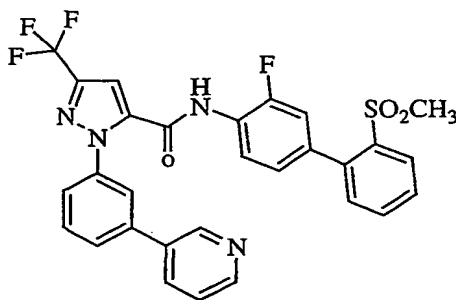


Part A: 1-(3-Cyanophenyl)-3-trifluoromethylpyrazole-5-carboxylic acid was prepared according the methods of WO98/28269 (see Example 14). The pyrazole acid chloride (0.51 mmol) was coupled with 2-methyl-4-imidazoloaniline (1.04 g, 2.25 mmol) using DMAP (0.31 g, 2.49 mmol) in 10 mL dichloromethane. After 24H the reaction mixture was concentrated. The resulting concentrate was dissolved in EtOAc and washed three times with brine. The organics were dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. The crude coupling product was used directly. LRMS: m/z 437 (M+H).

Part B: The crude benzonitrile was treated with thiosemicarbazide (0.04 g, 0.45 mmol) in 5 mL refluxing TFA for 4h. The reaction mixture was concentrated and purified by HPLC to give the aminothiadiaazole.  $^1\text{HNMR}$  (DMSO, 300MHz)  $\delta$ : 11.07 (s, 1H), 7.95 (s, 1H), 7.89-7.84 (m, 4H), 7.77 (d, 1H, J=2Hz), 7.71 (s, 1H), 7.63-7.55 (m, 4H), 2.50 (s, 3H)ppm; LRMS: m/z 256 (M/2+H), 511 (M+H); HRMS: calc'd for  $\text{C}_{23}\text{H}_{18}\text{SO}_2\text{N}_8$  511.1288.

#### Example 7

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole trifluoroacetic acid salt

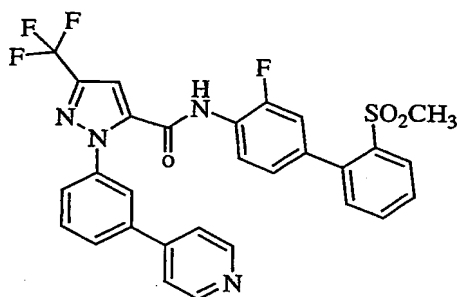


1-(Bromophenyl)-5-(2'-methylsulfonyl-[1,1']-biphen-4-yl)-3-trifluoromethyl-pyrazole was prepared according to the

methods of WO98/28269 (see Example 10, except that 3-methoxy-trichloroacetyl-4,4,4-trifluorocrotonate was used in place of 3-methoxy-trichloroacetylcrotonate). 3-Pyridylboronate (0.112 g, 0.75 mmol) was added to 1-(bromophenyl)-5-(2'-methylsulfonyl-[1,1']-biphen-4-yl)-3-trifluoromethyl-pyrazole (0.366 g, 0.62 mmol) in a solution of Toluene:EtOH (4:1, 50 mL). Sodium carbonate (2M, 0.4 mL) was added and the solution was degassed for 0.5h. To this solution was added Pd(PPh<sub>3</sub>)<sub>4</sub> and the solution was gently refluxed for 18h. The solution was concentrated and purified via reverse phase HPLC to afford 0.050g of colorless product. LRMS 581 m/z (rel. intensity), 581 (M+H, 100).

#### Example 8

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole trifluoroacetic acid salt

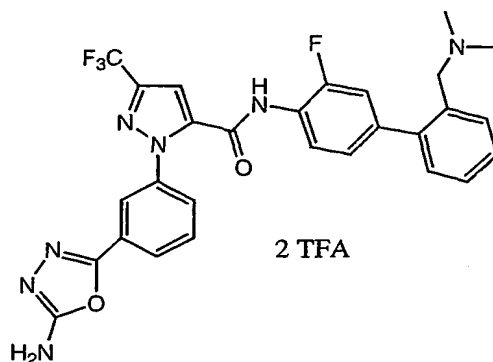


Prepared via the Stille coupling methodology using 4-tributyltinpyridine and the bromophenyl-pyrazole intermediate used in Example 8. The title compound was obtained as colorless crystals (20% yield) after purification by reverse phase HPLC. LRMS m/z (rel. intensity) 581 (M+H, 100).

25

#### Example 9

1-[3-(5-Amino-1,3,4-oxadiazol-2-yl)phenyl]-N-{2'-[(dimethylamino)methyl]-3-fluoro-1,1'-biphenyl-4-yl}-3-(trifluoromethyl)-1H-pyrazole-5-carboxamide

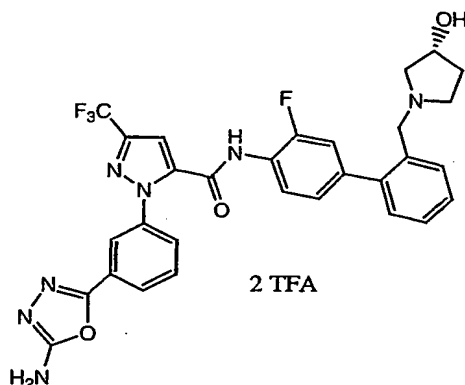


This compound was prepared by the methods described in Example 1-6. LRMS ( $ES^+$ ), 566.2 ( $M+H$ ) $^+$ .

5

#### Example 10

1-[3-(5-Amino-1,3,4-oxadiazol-2-yl)phenyl]-N-(3-fluoro-2'-  
 {[(3S)-3-hydroxy-1-pyrrolidinyl]methyl}-1,1'-biphenyl-4-yl)-  
 3-(trifluoromethyl)-1H-pyrazole-5-carboxamide

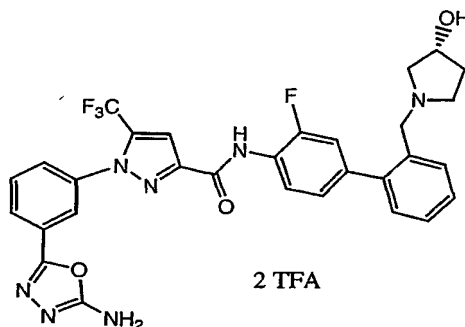


10

This compound was prepared by the methods described in Example 1-6. LRMS ( $ES^+$ ), 608.4 ( $M+H$ ) $^+$ .

#### Example 11

1-[3-(5-Amino-1,3,4-oxadiazol-2-yl)phenyl]-N-(3-fluoro-2'-  
 15 {[(3S)-3-hydroxy-1-pyrrolidinyl]methyl}-1,1'-biphenyl-4-yl)-  
 5-(trifluoromethyl)-1H-pyrazole-3-carboxamide



This compound was prepared by the methods described in Example 1-6. LRMS ( $ES^+$ ), 608.1 ( $M+H$ ) $^+$ .

- 5        The following tables contain representative examples of the present invention. Each entry in each table is intended to be paired with each formulas at the start of the table. For example, in Tables 1 and 2, example 1 is intended to be paired with each of the formulas.
- 10       The following nomenclature is intended for group A in the following tables.

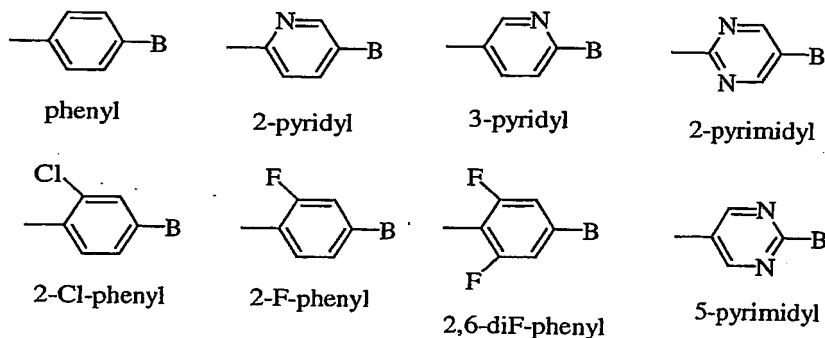
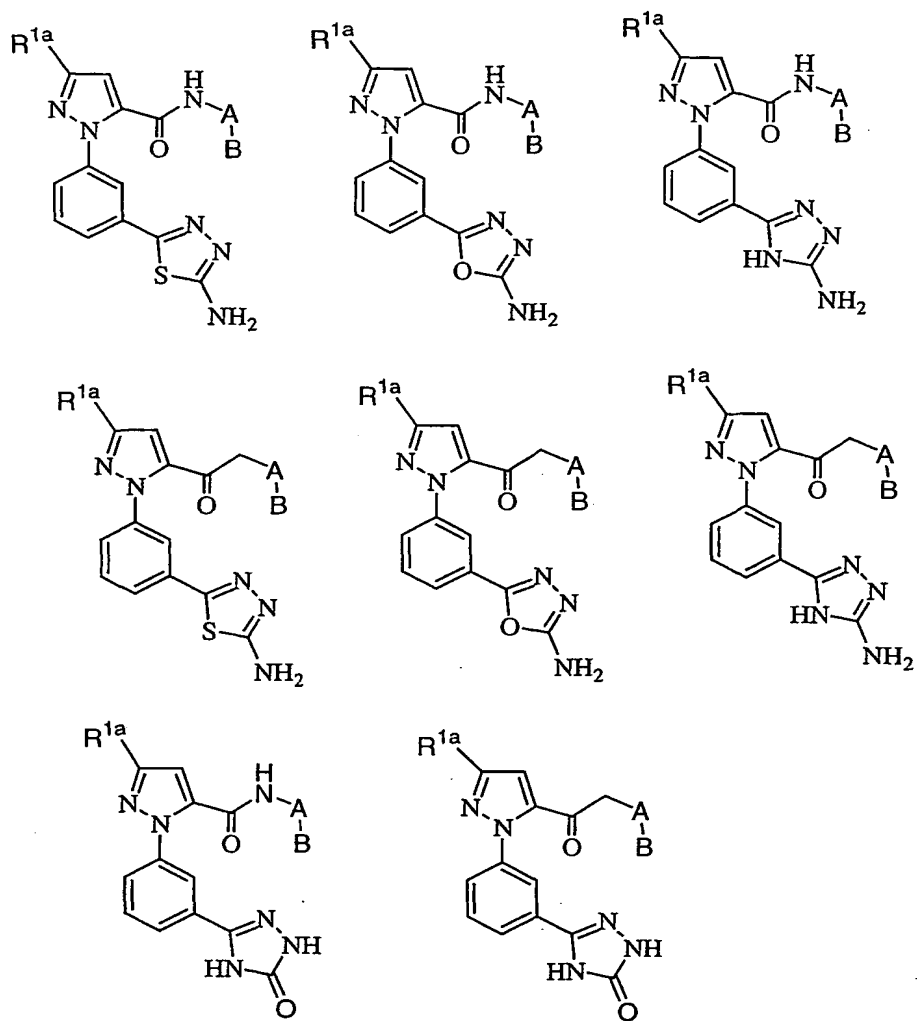
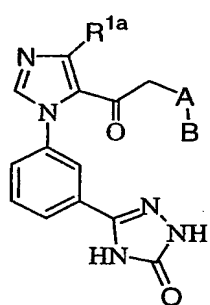
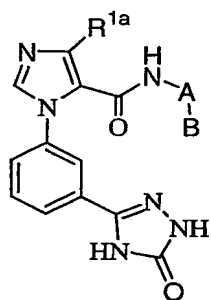
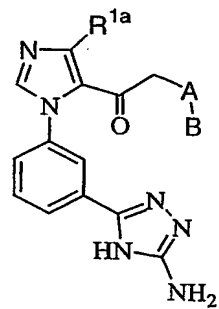
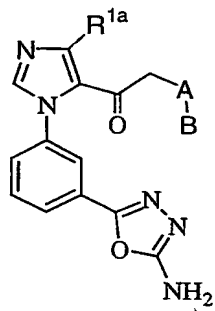
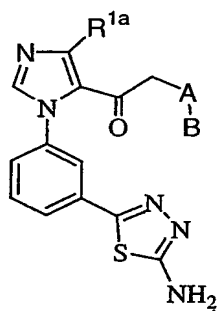
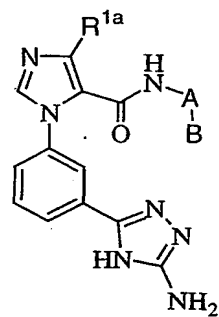
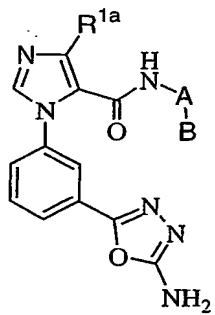
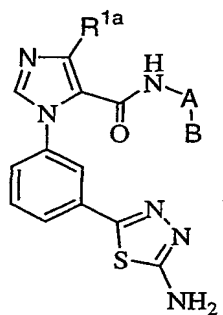
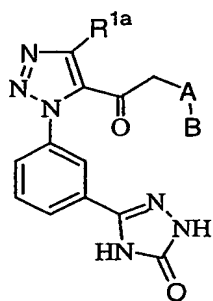
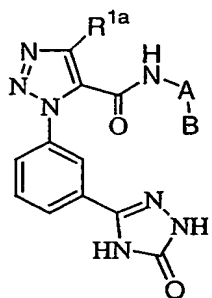
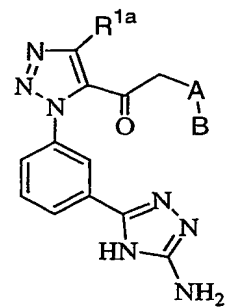
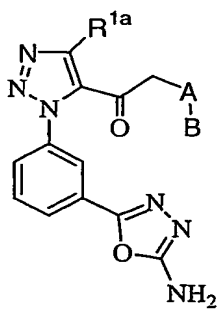
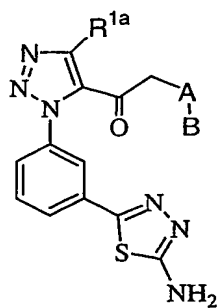
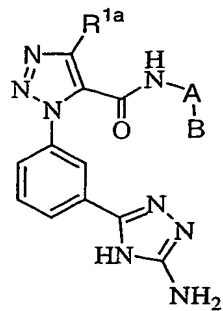
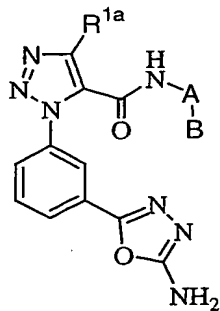
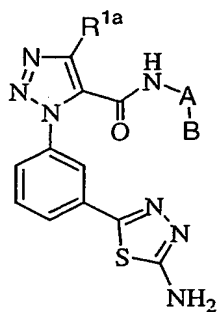
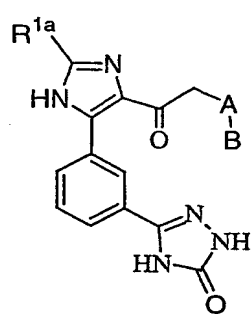
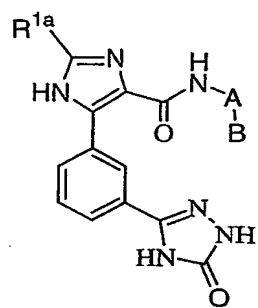
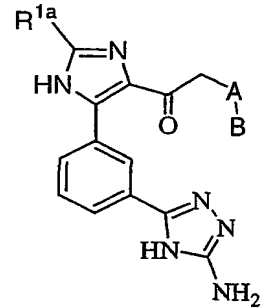
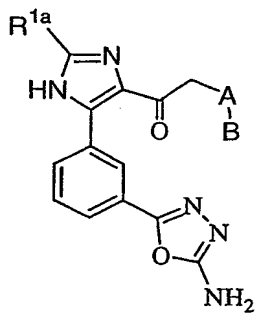
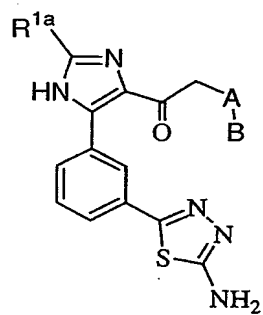
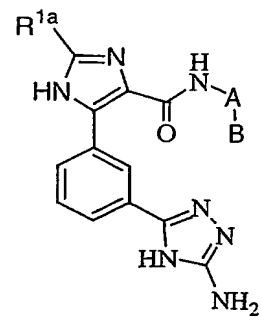
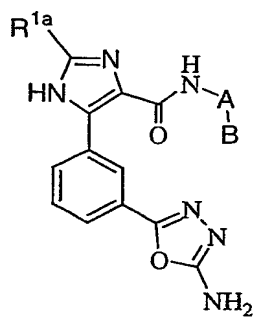
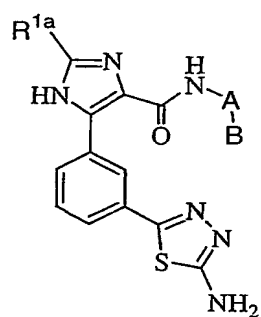


Table 1

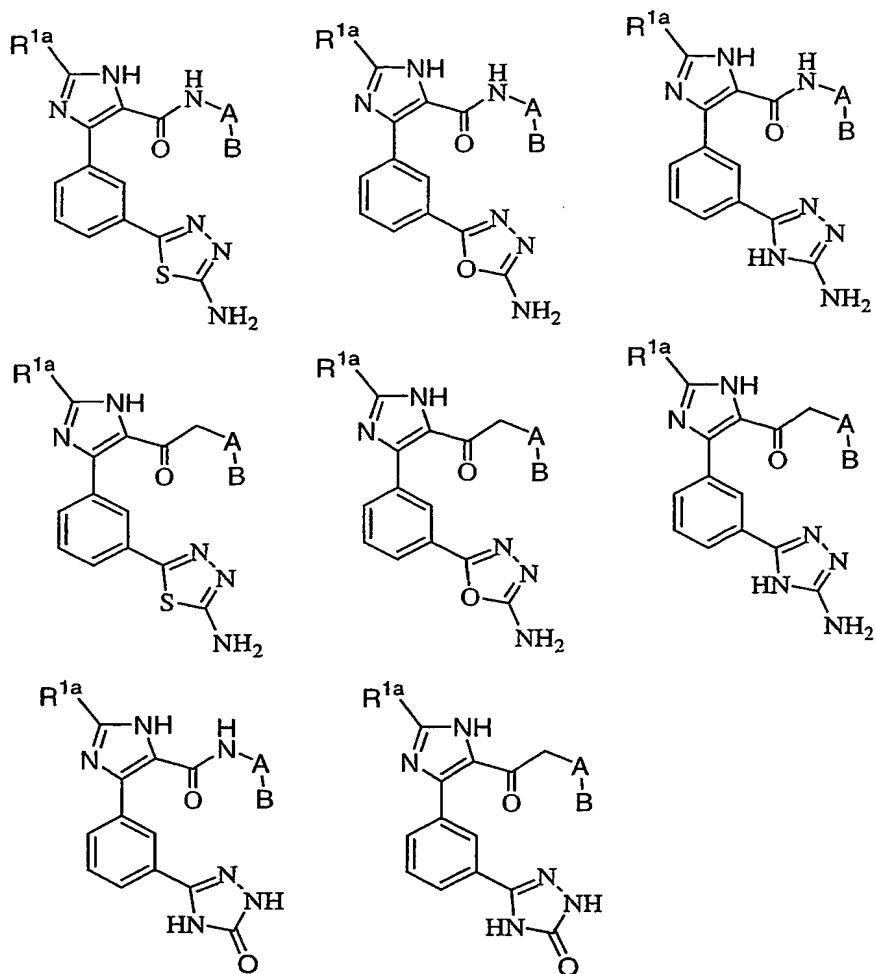


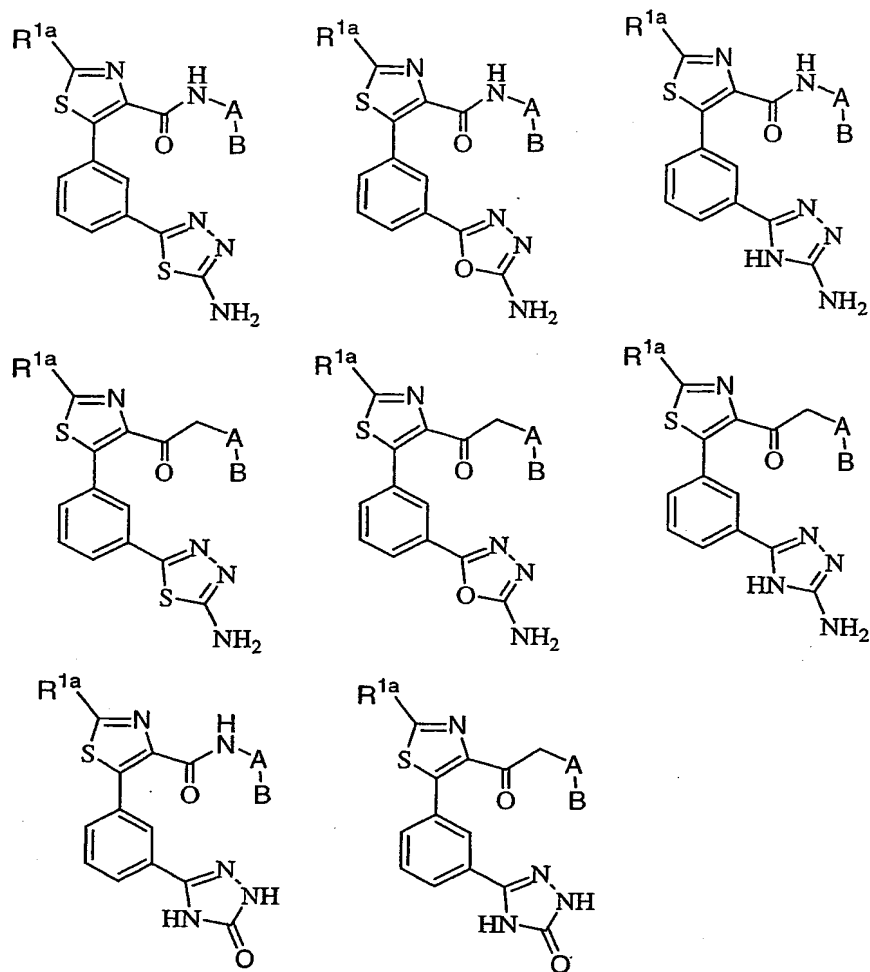


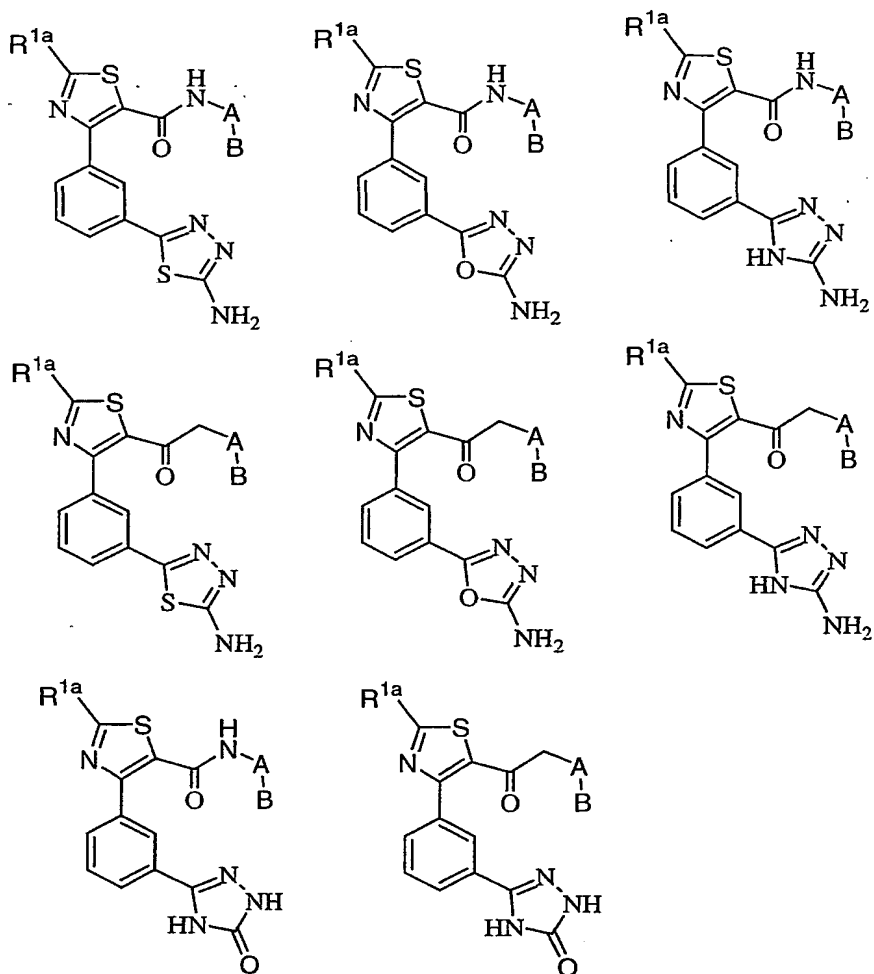












$R^{1a}$  is  $CH_3$ ;

5	Ex#	A	B
	1.	phenyl	2-( $NH_2SO_2$ )phenyl
	2.	phenyl	2-( $CH_3SO_2$ )phenyl
	3.	phenyl	3- $NH_2SO_2$ -4-pyridyl
	4.	phenyl	3- $CH_3SO_2$ -4-pyridyl
10	5.	phenyl	2-( $CH_3NH$ )phenyl
	6.	phenyl	3-(( $CH_3$ ) $_2NCH_2$ )-4-pyridyl
	7.	phenyl	2-(N-(3-R-HO-pyrrolidinyl) $CH_2$ )phenyl
	8.	phenyl	2-(N-(4-HO-piperidinyl) $CH_2$ )phenyl
	9.	phenyl	2-(( $CH_3$ ) $_2NCH_2$ )phenyl
15	10.	phenyl	2-(( $CH_3$ ) $NHCH_2$ )phenyl
	11.	phenyl	2-(( $CH_3CH_2$ ) $NHCH_2$ )phenyl
	12.	phenyl	2-(( $CH_3CH_2$ ) $_2NCH_2$ )phenyl
	13.	phenyl	2-(( $CH_3CH_2$ )N( $CH_3$ ) $CH_2$ )phenyl
	14.	phenyl	2-((( $CH_3$ ) $_2CH$ ) $NHCH_2$ )phenyl
20	15.	phenyl	2-((( $CH_3$ ) $_2CH$ ) $_2NCH_2$ )phenyl
	16.	phenyl	2-((cyclopropyl) $NHCH_2$ )phenyl

	17.	phenyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	18.	phenyl	2-((cyclobutyl)NHCH <sub>2</sub> )phenyl
	19.	phenyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
5	20.	phenyl	2-((cyclopentyl)NHCH <sub>2</sub> )phenyl
	21.	phenyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	22.	phenyl	2-((cyclohexyl)NHCH <sub>2</sub> )phenyl
	23.	phenyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	24.	phenyl	1-CH <sub>3</sub> -2-imidazolyl
	25.	phenyl	2-CH <sub>3</sub> -1-imidazolyl
10	26.	phenyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	27.	phenyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	28.	phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	29.	phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
15	30.	phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )-1-imidazolyl
	31.	phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )-1-imidazolyl
	32.	phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	33.	phenyl	2-((cyclopropyl)NHCH <sub>2</sub> )-1-imidazolyl
	34.	phenyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	35.	phenyl	2-((cyclobutyl)NHCH <sub>2</sub> )-1-imidazolyl
20	36.	phenyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	37.	phenyl	2-((cyclopentyl)NHCH <sub>2</sub> )-1-imidazolyl
	38.	phenyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	39.	phenyl	2-((cyclohexyl)NHCH <sub>2</sub> )-1-imidazolyl
	40.	phenyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
25	41.	2-pyridyl	2-(NH <sub>2</sub> SO <sub>2</sub> )phenyl
	42.	2-pyridyl	2-(CH <sub>3</sub> SO <sub>2</sub> )phenyl
	43.	2-pyridyl	3-NH <sub>2</sub> SO <sub>2</sub> -4-pyridyl
	44.	2-pyridyl	3-CH <sub>3</sub> SO <sub>2</sub> -4-pyridyl
	45.	2-pyridyl	2-(CH <sub>3</sub> NH)phenyl
30	46.	2-pyridyl	3-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-4-pyridyl
	47.	2-pyridyl	2-(N-(3-R-HO-pyrrolidinyl)CH <sub>2</sub> )phenyl
	48.	2-pyridyl	2-(N-(4-HO-piperidinyl)CH <sub>2</sub> )phenyl
	49.	2-pyridyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
	50.	2-pyridyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )phenyl
35	51.	2-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )phenyl
	52.	2-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
	53.	2-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )phenyl
	54.	2-pyridyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )phenyl
	55.	2-pyridyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )phenyl
40	56.	2-pyridyl	2-((cyclopropyl)NHCH <sub>2</sub> )phenyl
	57.	2-pyridyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	58.	2-pyridyl	2-((cyclobutyl)NHCH <sub>2</sub> )phenyl
	59.	2-pyridyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	60.	2-pyridyl	2-((cyclopentyl)NHCH <sub>2</sub> )phenyl
45	61.	2-pyridyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	62.	2-pyridyl	2-((cyclohexyl)NHCH <sub>2</sub> )phenyl
	63.	2-pyridyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	64.	2-pyridyl	1-CH <sub>3</sub> -2-imidazolyl
	65.	2-pyridyl	2-CH <sub>3</sub> -1-imidazolyl
50	66.	2-pyridyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	67.	2-pyridyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	68.	2-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	69.	2-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl

	70.	2-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )-1-imidazolyl
	71.	2-pyridyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )-1-imidazolyl
	72.	2-pyridyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	73.	2-pyridyl	2-((cyclopropyl)NHCH <sub>2</sub> )-1-imidazolyl
5	74.	2-pyridyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	75.	2-pyridyl	2-((cyclobutyl)NHCH <sub>2</sub> )-1-imidazolyl
	76.	2-pyridyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	77.	2-pyridyl	2-((cyclopentyl)NHCH <sub>2</sub> )-1-imidazolyl
	78.	2-pyridyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
10	79.	2-pyridyl	2-((cyclohexyl)NHCH <sub>2</sub> )-1-imidazolyl
	80.	2-pyridyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	81.	3-pyridyl	2-(NH <sub>2</sub> SO <sub>2</sub> )phenyl
	82.	3-pyridyl	2-(CH <sub>3</sub> SO <sub>2</sub> )phenyl
	83.	3-pyridyl	3-NH <sub>2</sub> SO <sub>2</sub> -4-pyridyl
15	84.	3-pyridyl	3-CH <sub>3</sub> SO <sub>2</sub> -4-pyridyl
	85.	3-pyridyl	2-(CH <sub>3</sub> NH)phenyl
	86.	3-pyridyl	3-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-4-pyridyl
	87.	3-pyridyl	2-(N-(3-R-HO-pyrrolidinyl)CH <sub>2</sub> )phenyl
	88.	3-pyridyl	2-(N-(4-HO-piperidinyl)CH <sub>2</sub> )phenyl
20	89.	3-pyridyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
	90.	3-pyridyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )phenyl
	91.	3-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )phenyl
	92.	3-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
	93.	3-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )phenyl
25	94.	3-pyridyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )phenyl
	95.	3-pyridyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )phenyl
	96.	3-pyridyl	2-((cyclopropyl)NHCH <sub>2</sub> )phenyl
	97.	3-pyridyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	98.	3-pyridyl	2-((cyclobutyl)NHCH <sub>2</sub> )phenyl
30	99.	3-pyridyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	100.	3-pyridyl	2-((cyclopentyl)NHCH <sub>2</sub> )phenyl
	101.	3-pyridyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	102.	3-pyridyl	2-((cyclohexyl)NHCH <sub>2</sub> )phenyl
	103.	3-pyridyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
35	104.	3-pyridyl	1-CH <sub>3</sub> -2-imidazolyl
	105.	3-pyridyl	2-CH <sub>3</sub> -1-imidazolyl
	106.	3-pyridyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	107.	3-pyridyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	108.	3-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )-1-imidazolyl
40	109.	3-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	110.	3-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )-1-imidazolyl
	111.	3-pyridyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )-1-imidazolyl
	112.	3-pyridyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	113.	3-pyridyl	2-((cyclopropyl)NHCH <sub>2</sub> )-1-imidazolyl
45	114.	3-pyridyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	115.	3-pyridyl	2-((cyclobutyl)NHCH <sub>2</sub> )-1-imidazolyl
	116.	3-pyridyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	117.	3-pyridyl	2-((cyclopentyl)NHCH <sub>2</sub> )-1-imidazolyl
	118.	3-pyridyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
50	119.	3-pyridyl	2-((cyclohexyl)NHCH <sub>2</sub> )-1-imidazolyl
	120.	3-pyridyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	121.	2-pyrimidyl	2-(NH <sub>2</sub> SO <sub>2</sub> )phenyl
	122.	2-pyrimidyl	2-(CH <sub>3</sub> SO <sub>2</sub> )phenyl

123. 2-pyrimidyl 3-NH<sub>2</sub>SO<sub>2</sub>-4-pyridyl  
124. 2-pyrimidyl 3-CH<sub>3</sub>SO<sub>2</sub>-4-pyridyl  
125. 2-pyrimidyl 2-(CH<sub>3</sub>NH)phenyl  
126. 2-pyrimidyl 3-((CH<sub>3</sub>)<sub>2</sub>NCH<sub>2</sub>)-4-pyridyl  
5 127. 2-pyrimidyl 2-(N-(3-R-HO-pyrrolidinyl)CH<sub>2</sub>)phenyl  
128. 2-pyrimidyl 2-(N-(4-HO-piperidinyl)CH<sub>2</sub>)phenyl  
129. 2-pyrimidyl 2-((CH<sub>3</sub>)<sub>2</sub>NCH<sub>2</sub>)phenyl  
130. 2-pyrimidyl 2-((CH<sub>3</sub>)NHCH<sub>2</sub>)phenyl  
131. 2-pyrimidyl 2-((CH<sub>3</sub>CH<sub>2</sub>)NHCH<sub>2</sub>)phenyl  
10 132. 2-pyrimidyl 2-((CH<sub>3</sub>CH<sub>2</sub>)<sub>2</sub>NCH<sub>2</sub>)phenyl  
133. 2-pyrimidyl 2-((CH<sub>3</sub>CH<sub>2</sub>)N(CH<sub>3</sub>)CH<sub>2</sub>)phenyl  
134. 2-pyrimidyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)NHCH<sub>2</sub>)phenyl  
135. 2-pyrimidyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)<sub>2</sub>NCH<sub>2</sub>)phenyl  
136. 2-pyrimidyl 2-((cyclopropyl)NHCH<sub>2</sub>)phenyl  
15 137. 2-pyrimidyl 2-((cyclopropyl)<sub>2</sub>NCH<sub>2</sub>)phenyl  
138. 2-pyrimidyl 2-((cyclobutyl)NHCH<sub>2</sub>)phenyl  
139. 2-pyrimidyl 2-((cyclobutyl)<sub>2</sub>NCH<sub>2</sub>)phenyl  
140. 2-pyrimidyl 2-((cyclopentyl)NHCH<sub>2</sub>)phenyl  
141. 2-pyrimidyl 2-((cyclopentyl)<sub>2</sub>NCH<sub>2</sub>)phenyl  
20 142. 2-pyrimidyl 2-((cyclohexyl)NHCH<sub>2</sub>)phenyl  
143. 2-pyrimidyl 2-((cyclohexyl)<sub>2</sub>NCH<sub>2</sub>)phenyl  
144. 2-pyrimidyl 1-CH<sub>3</sub>-2-imidazolyl  
145. 2-pyrimidyl 2-CH<sub>3</sub>-1-imidazolyl  
146. 2-pyrimidyl 2-((CH<sub>3</sub>)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
25 147. 2-pyrimidyl 2-((CH<sub>3</sub>)NHCH<sub>2</sub>)-1-imidazolyl  
148. 2-pyrimidyl 2-((CH<sub>3</sub>CH<sub>2</sub>)NHCH<sub>2</sub>)-1-imidazolyl  
149. 2-pyrimidyl 2-((CH<sub>3</sub>CH<sub>2</sub>)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
150. 2-pyrimidyl 2-((CH<sub>3</sub>CH<sub>2</sub>)N(CH<sub>3</sub>)CH<sub>2</sub>)-1-imidazolyl  
151. 2-pyrimidyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)NHCH<sub>2</sub>)-1-imidazolyl  
30 152. 2-pyrimidyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
153. 2-pyrimidyl 2-((cyclopropyl)NHCH<sub>2</sub>)-1-imidazolyl  
154. 2-pyrimidyl 2-((cyclopropyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
155. 2-pyrimidyl 2-((cyclobutyl)NHCH<sub>2</sub>)-1-imidazolyl  
156. 2-pyrimidyl 2-((cyclobutyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
35 157. 2-pyrimidyl 2-((cyclopentyl)NHCH<sub>2</sub>)-1-imidazolyl  
158. 2-pyrimidyl 2-((cyclopentyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
159. 2-pyrimidyl 2-((cyclohexyl)NHCH<sub>2</sub>)-1-imidazolyl  
160. 2-pyrimidyl 2-((cyclohexyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
161. 5-pyrimidyl 2-(NH<sub>2</sub>SO<sub>2</sub>)phenyl  
40 162. 5-pyrimidyl 2-(CH<sub>3</sub>SO<sub>2</sub>)phenyl  
163. 5-pyrimidyl 3-NH<sub>2</sub>SO<sub>2</sub>-4-pyridyl  
164. 5-pyrimidyl 3-CH<sub>3</sub>SO<sub>2</sub>-4-pyridyl  
165. 5-pyrimidyl 2-(CH<sub>3</sub>NH)phenyl  
166. 5-pyrimidyl 3-((CH<sub>3</sub>)<sub>2</sub>NCH<sub>2</sub>)-4-pyridyl  
45 167. 5-pyrimidyl 2-(N-(3-R-HO-pyrrolidinyl)CH<sub>2</sub>)phenyl  
168. 5-pyrimidyl 2-(N-(4-HO-piperidinyl)CH<sub>2</sub>)phenyl  
169. 5-pyrimidyl 2-((CH<sub>3</sub>)<sub>2</sub>NCH<sub>2</sub>)phenyl  
170. 5-pyrimidyl 2-((CH<sub>3</sub>)NHCH<sub>2</sub>)phenyl  
171. 5-pyrimidyl 2-((CH<sub>3</sub>CH<sub>2</sub>)NHCH<sub>2</sub>)phenyl  
50 172. 5-pyrimidyl 2-((CH<sub>3</sub>CH<sub>2</sub>)<sub>2</sub>NCH<sub>2</sub>)phenyl  
173. 5-pyrimidyl 2-((CH<sub>3</sub>CH<sub>2</sub>)N(CH<sub>3</sub>)CH<sub>2</sub>)phenyl  
174. 5-pyrimidyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)NHCH<sub>2</sub>)phenyl  
175. 5-pyrimidyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)<sub>2</sub>NCH<sub>2</sub>)phenyl

	176.	5-pyrimidyl	2-((cyclopropyl)NHCH <sub>2</sub> )phenyl
	177.	5-pyrimidyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	178.	5-pyrimidyl	2-((cyclobutyl)NHCH <sub>2</sub> )phenyl
	179.	5-pyrimidyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
5	180.	5-pyrimidyl	2-((cyclopentyl)NHCH <sub>2</sub> )phenyl
	181.	5-pyrimidyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	182.	5-pyrimidyl	2-((cyclohexyl)NHCH <sub>2</sub> )phenyl
	183.	5-pyrimidyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	184.	5-pyrimidyl	1-CH <sub>3</sub> -2-imidazolyl
10	185.	5-pyrimidyl	2-CH <sub>3</sub> -1-imidazolyl
	186.	5-pyrimidyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	187.	5-pyrimidyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	188.	5-pyrimidyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	189.	5-pyrimidyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
15	190.	5-pyrimidyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )-1-imidazolyl
	191.	5-pyrimidyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )-1-imidazolyl
	192.	5-pyrimidyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	193.	5-pyrimidyl	2-((cyclopropyl)NHCH <sub>2</sub> )-1-imidazolyl
	194.	5-pyrimidyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
20	195.	5-pyrimidyl	2-((cyclobutyl)NHCH <sub>2</sub> )-1-imidazolyl
	196.	5-pyrimidyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	197.	5-pyrimidyl	2-((cyclopentyl)NHCH <sub>2</sub> )-1-imidazolyl
	198.	5-pyrimidyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	199.	5-pyrimidyl	2-((cyclohexyl)NHCH <sub>2</sub> )-1-imidazolyl
25	200.	5-pyrimidyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	201.	2-Cl-phenyl	2-(NH <sub>2</sub> SO <sub>2</sub> )phenyl
	202.	2-Cl-phenyl	2-(CH <sub>3</sub> SO <sub>2</sub> )phenyl
	203.	2-Cl-phenyl	3-NH <sub>2</sub> SO <sub>2</sub> -4-pyridyl
	204.	2-Cl-phenyl	3-CH <sub>3</sub> SO <sub>2</sub> -4-pyridyl
30	205.	2-Cl-phenyl	2-(CH <sub>3</sub> NH)phenyl
	206.	2-Cl-phenyl	3-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-4-pyridyl
	207.	2-Cl-phenyl	2-(N-(3-R-HO-pyrrolidinyl)CH <sub>2</sub> )phenyl
	208.	2-Cl-phenyl	2-(N-(4-HO-piperidinyl)CH <sub>2</sub> )phenyl
	209.	2-Cl-phenyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
35	210.	2-Cl-phenyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )phenyl
	211.	2-Cl-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )phenyl
	212.	2-Cl-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
	213.	2-Cl-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )phenyl
	214.	2-Cl-phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )phenyl
40	215.	2-Cl-phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )phenyl
	216.	2-Cl-phenyl	2-((cyclopropyl)NHCH <sub>2</sub> )phenyl
	217.	2-Cl-phenyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	218.	2-Cl-phenyl	2-((cyclobutyl)NHCH <sub>2</sub> )phenyl
	219.	2-Cl-phenyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
45	220.	2-Cl-phenyl	2-((cyclopentyl)NHCH <sub>2</sub> )phenyl
	221.	2-Cl-phenyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	222.	2-Cl-phenyl	2-((cyclohexyl)NHCH <sub>2</sub> )phenyl
	223.	2-Cl-phenyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	224.	2-Cl-phenyl	1-CH <sub>3</sub> -2-imidazolyl
50	225.	2-Cl-phenyl	2-CH <sub>3</sub> -1-imidazolyl
	226.	2-Cl-phenyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	227.	2-Cl-phenyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	228.	2-Cl-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )-1-imidazolyl

229. 2-Cl-phenyl 2-((CH<sub>3</sub>CH<sub>2</sub>)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
 230. 2-Cl-phenyl 2-((CH<sub>3</sub>CH<sub>2</sub>)N(CH<sub>3</sub>)CH<sub>2</sub>)-1-imidazolyl  
 231. 2-Cl-phenyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)NHCH<sub>2</sub>)-1-imidazolyl  
 232. 2-Cl-phenyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
 5 233. 2-Cl-phenyl 2-((cyclopropyl)NHCH<sub>2</sub>)-1-imidazolyl  
 234. 2-Cl-phenyl 2-((cyclopropyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
 235. 2-Cl-phenyl 2-((cyclobutyl)NHCH<sub>2</sub>)-1-imidazolyl  
 236. 2-Cl-phenyl 2-((cyclobutyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
 10 237. 2-Cl-phenyl 2-((cyclopentyl)NHCH<sub>2</sub>)-1-imidazolyl  
 238. 2-Cl-phenyl 2-((cyclopentyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
 239. 2-Cl-phenyl 2-((cyclohexyl)NHCH<sub>2</sub>)-1-imidazolyl  
 240. 2-Cl-phenyl 2-((cyclohexyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
 241. 2-F-phenyl 2-(NH<sub>2</sub>SO<sub>2</sub>)phenyl  
 242. 2-F-phenyl 2-(CH<sub>3</sub>SO<sub>2</sub>)phenyl  
 15 243. 2-F-phenyl 3-NH<sub>2</sub>SO<sub>2</sub>-4-pyridyl  
 244. 2-F-phenyl 3-CH<sub>3</sub>SO<sub>2</sub>-4-pyridyl  
 245. 2-F-phenyl 2-(CH<sub>3</sub>NH)phenyl  
 246. 2-F-phenyl 3-((CH<sub>3</sub>)<sub>2</sub>NCH<sub>2</sub>)-4-pyridyl  
 247. 2-F-phenyl 2-(N-(3-R-HO-pyrrolidinyl)CH<sub>2</sub>)phenyl  
 20 248. 2-F-phenyl 2-(N-(4-HO-piperidinyl)CH<sub>2</sub>)phenyl  
 249. 2-F-phenyl 2-((CH<sub>3</sub>)<sub>2</sub>NCH<sub>2</sub>)phenyl  
 250. 2-F-phenyl 2-((CH<sub>3</sub>)NHCH<sub>2</sub>)phenyl  
 251. 2-F-phenyl 2-((CH<sub>3</sub>CH<sub>2</sub>)NHCH<sub>2</sub>)phenyl  
 252. 2-F-phenyl 2-((CH<sub>3</sub>CH<sub>2</sub>)<sub>2</sub>NCH<sub>2</sub>)phenyl  
 25 253. 2-F-phenyl 2-((CH<sub>3</sub>CH<sub>2</sub>)N(CH<sub>3</sub>)CH<sub>2</sub>)phenyl  
 254. 2-F-phenyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)NHCH<sub>2</sub>)phenyl  
 255. 2-F-phenyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)<sub>2</sub>NCH<sub>2</sub>)phenyl  
 256. 2-F-phenyl 2-((cyclopropyl)NHCH<sub>2</sub>)phenyl  
 257. 2-F-phenyl 2-((cyclopropyl)<sub>2</sub>NCH<sub>2</sub>)phenyl  
 30 258. 2-F-phenyl 2-((cyclobutyl)NHCH<sub>2</sub>)phenyl  
 259. 2-F-phenyl 2-((cyclobutyl)<sub>2</sub>NCH<sub>2</sub>)phenyl  
 260. 2-F-phenyl 2-((cyclopentyl)NHCH<sub>2</sub>)phenyl  
 261. 2-F-phenyl 2-((cyclopentyl)<sub>2</sub>NCH<sub>2</sub>)phenyl  
 262. 2-F-phenyl 2-((cyclohexyl)NHCH<sub>2</sub>)phenyl  
 35 263. 2-F-phenyl 2-((cyclohexyl)<sub>2</sub>NCH<sub>2</sub>)phenyl  
 264. 2-F-phenyl 1-CH<sub>3</sub>-2-imidazolyl  
 265. 2-F-phenyl 2-CH<sub>3</sub>-1-imidazolyl  
 266. 2-F-phenyl 2-((CH<sub>3</sub>)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
 267. 2-F-phenyl 2-((CH<sub>3</sub>)NHCH<sub>2</sub>)-1-imidazolyl  
 40 268. 2-F-phenyl 2-((CH<sub>3</sub>CH<sub>2</sub>)NHCH<sub>2</sub>)-1-imidazolyl  
 269. 2-F-phenyl 2-((CH<sub>3</sub>CH<sub>2</sub>)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
 270. 2-F-phenyl 2-((CH<sub>3</sub>CH<sub>2</sub>)N(CH<sub>3</sub>)CH<sub>2</sub>)-1-imidazolyl  
 271. 2-F-phenyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)NHCH<sub>2</sub>)-1-imidazolyl  
 272. 2-F-phenyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
 45 273. 2-F-phenyl 2-((cyclopropyl)NHCH<sub>2</sub>)-1-imidazolyl  
 274. 2-F-phenyl 2-((cyclopropyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
 275. 2-F-phenyl 2-((cyclobutyl)NHCH<sub>2</sub>)-1-imidazolyl  
 276. 2-F-phenyl 2-((cyclobutyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
 277. 2-F-phenyl 2-((cyclopentyl)NHCH<sub>2</sub>)-1-imidazolyl  
 50 278. 2-F-phenyl 2-((cyclopentyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
 279. 2-F-phenyl 2-((cyclohexyl)NHCH<sub>2</sub>)-1-imidazolyl  
 280. 2-F-phenyl 2-((cyclohexyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
 281. 2,6-diF-phenyl 2-(NH<sub>2</sub>SO<sub>2</sub>)phenyl



	282.	2,6-diF-phenyl	2-(CH <sub>3</sub> SO <sub>2</sub> )phenyl
	283.	2,6-diF-phenyl	3-NH <sub>2</sub> SO <sub>2</sub> -4-pyridyl
	284.	2,6-diF-phenyl	3-CH <sub>3</sub> SO <sub>2</sub> -4-pyridyl
	285.	2,6-diF-phenyl	2-(CH <sub>3</sub> NH)phenyl
5	286.	2,6-diF-phenyl	3-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-4-pyridyl
	287.	2,6-diF-phenyl	2-(N-(3-R-HO-pyrrolidinyl)CH <sub>2</sub> )phenyl
	288.	2,6-diF-phenyl	2-(N-(4-HO-piperidinyl)CH <sub>2</sub> )phenyl
	289.	2,6-diF-phenyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
	290.	2,6-diF-phenyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )phenyl
10	291.	2,6-diF-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )phenyl
	292.	2,6-diF-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
	293.	2,6-diF-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )phenyl
	294.	2,6-diF-phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )phenyl
	295.	2,6-diF-phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )phenyl
15	296.	2,6-diF-phenyl	2-((cyclopropyl)NHCH <sub>2</sub> )phenyl
	297.	2,6-diF-phenyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	298.	2,6-diF-phenyl	2-((cyclobutyl)NHCH <sub>2</sub> )phenyl
	299.	2,6-diF-phenyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	300.	2,6-diF-phenyl	2-((cyclopentyl)NHCH <sub>2</sub> )phenyl
20	301.	2,6-diF-phenyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	302.	2,6-diF-phenyl	2-((cyclohexyl)NHCH <sub>2</sub> )phenyl
	303.	2,6-diF-phenyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	304.	2,6-diF-phenyl	1-CH <sub>3</sub> -2-imidazolyl
	305.	2,6-diF-phenyl	2-CH <sub>3</sub> -1-imidazolyl
25	306.	2,6-diF-phenyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	307.	2,6-diF-phenyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	308.	2,6-diF-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	309.	2,6-diF-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	310.	2,6-diF-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )-1-imidazolyl
30	311.	2,6-diF-phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )-1-imidazolyl
	312.	2,6-diF-phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	313.	2,6-diF-phenyl	2-((cyclopropyl)NHCH <sub>2</sub> )-1-imidazolyl
	314.	2,6-diF-phenyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	315.	2,6-diF-phenyl	2-((cyclobutyl)NHCH <sub>2</sub> )-1-imidazolyl
35	316.	2,6-diF-phenyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	317.	2,6-diF-phenyl	2-((cyclopentyl)NHCH <sub>2</sub> )-1-imidazolyl
	318.	2,6-diF-phenyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	319.	2,6-diF-phenyl	2-((cyclohexyl)NHCH <sub>2</sub> )-1-imidazolyl
	320.	2,6-diF-phenyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
40	321.	piperidinyl	2-(NH <sub>2</sub> SO <sub>2</sub> )phenyl
	322.	piperidinyl	2-(CH <sub>3</sub> SO <sub>2</sub> )phenyl
	323.	piperidinyl	3-NH <sub>2</sub> SO <sub>2</sub> -4-pyridyl
	324.	piperidinyl	3-CH <sub>3</sub> SO <sub>2</sub> -4-pyridyl
	325.	piperidinyl	2-(CH <sub>3</sub> NH)phenyl
45	326.	piperidinyl	3-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-4-pyridyl
	327.	piperidinyl	2-(N-(3-R-HO-pyrrolidinyl)CH <sub>2</sub> )phenyl
	328.	piperidinyl	2-(N-(4-HO-piperidinyl)CH <sub>2</sub> )phenyl
	329.	piperidinyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
	330.	piperidinyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )phenyl
50	331.	piperidinyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )phenyl
	332.	piperidinyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
	333.	piperidinyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )phenyl
	334.	piperidinyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )phenyl

335. piperidinyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)<sub>2</sub>NCH<sub>2</sub>)phenyl  
336. piperidinyl 2-((cyclopropyl)NHCH<sub>2</sub>)phenyl  
337. piperidinyl 2-((cyclopropyl)<sub>2</sub>NCH<sub>2</sub>)phenyl  
338. piperidinyl 2-((cyclobutyl)NHCH<sub>2</sub>)phenyl  
5 339. piperidinyl 2-((cyclobutyl)<sub>2</sub>NCH<sub>2</sub>)phenyl  
340. piperidinyl 2-((cyclopentyl)NHCH<sub>2</sub>)phenyl  
341. piperidinyl 2-((cyclopentyl)<sub>2</sub>NCH<sub>2</sub>)phenyl  
342. piperidinyl 2-((cyclohexyl)NHCH<sub>2</sub>)phenyl  
343. piperidinyl 2-((cyclohexyl)<sub>2</sub>NCH<sub>2</sub>)phenyl  
10 344. piperidinyl 1-CH<sub>3</sub>-2-imidazolyl  
345. piperidinyl 2-CH<sub>3</sub>-1-imidazolyl  
346. piperidinyl 2-((CH<sub>3</sub>)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
347. piperidinyl 2-((CH<sub>3</sub>)NHCH<sub>2</sub>)-1-imidazolyl  
348. piperidinyl 2-((CH<sub>3</sub>CH<sub>2</sub>)NHCH<sub>2</sub>)-1-imidazolyl  
15 349. piperidinyl 2-((CH<sub>3</sub>CH<sub>2</sub>)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
350. piperidinyl 2-((CH<sub>3</sub>CH<sub>2</sub>)N(CH<sub>3</sub>)CH<sub>2</sub>)-1-imidazolyl  
351. piperidinyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)NHCH<sub>2</sub>)-1-imidazolyl  
352. piperidinyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
353. piperidinyl 2-((cyclopropyl)NHCH<sub>2</sub>)-1-imidazolyl  
20 354. piperidinyl 2-((cyclopropyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
355. piperidinyl 2-((cyclobutyl)NHCH<sub>2</sub>)-1-imidazolyl  
356. piperidinyl 2-((cyclobutyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
357. piperidinyl 2-((cyclopentyl)NHCH<sub>2</sub>)-1-imidazolyl  
358. piperidinyl 2-((cyclopentyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
25 359. piperidinyl 2-((cyclohexyl)NHCH<sub>2</sub>)-1-imidazolyl  
360. piperidinyl 2-((cyclohexyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl

30

## Table 2

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

5         $R^{1a}$  is  $\text{CH}_2\text{CH}_3$ .

## Table 3

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

10

$R^{1a}$  is  $\text{CF}_3$ .

## Table 4

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

15

$R^{1a}$  is  $\text{SCH}_3$ .

## Table 5

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

20

$R^{1a}$  is  $\text{SOCH}_3$ .

## Table 6

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

25

$R^{1a}$  is  $\text{SO}_2\text{CH}_3$ .

30

## Table 7

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

35

$R^{1a}$  is  $\text{Cl}$ .

## Table 8

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

$R^{1a}$  is F.

## Table 9

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

$R^{1a}$  is  $\text{CO}_2\text{CH}_3$ .

## Table 10

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

$R^{1a}$  is  $\text{CH}_2\text{OCH}_3$ .

## Table 11

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

$R^{1a}$  is  $\text{CONH}_2$ .

## Table 12

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

$R^{1a}$  is CN.

## Table 13

Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

R<sup>1a</sup> is CH<sub>2</sub>NH<sub>2</sub>.

Table 14

5 Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

R<sup>1a</sup> is CH<sub>2</sub>NHSO<sub>2</sub>CH<sub>3</sub>.

Table 15

10 Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

R<sup>1a</sup> is 1-imidazolyl-CH<sub>2</sub>.

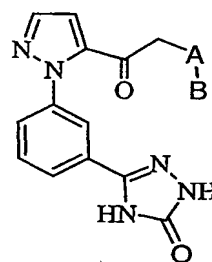
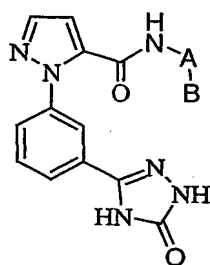
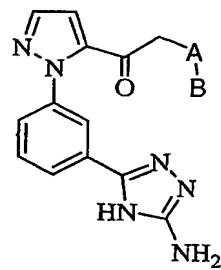
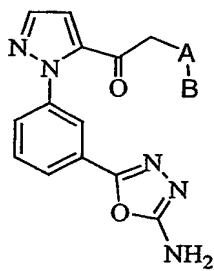
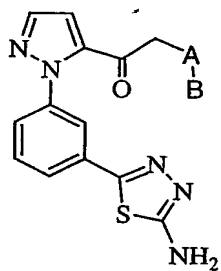
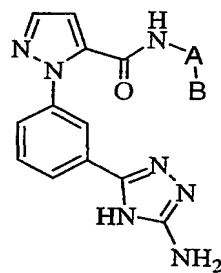
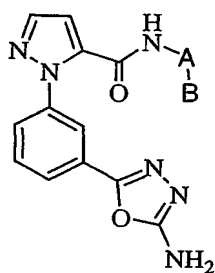
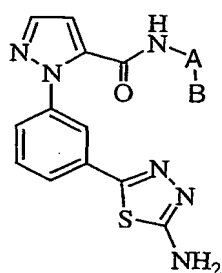
15 Table 16

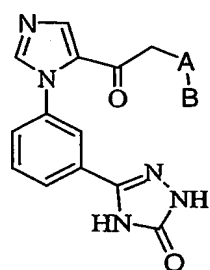
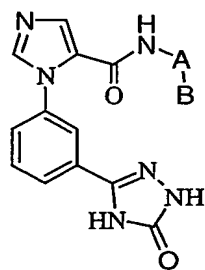
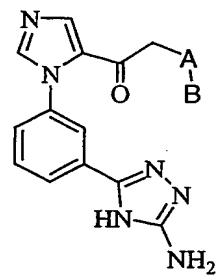
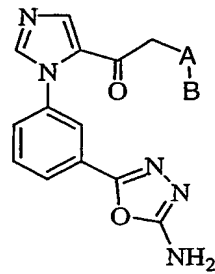
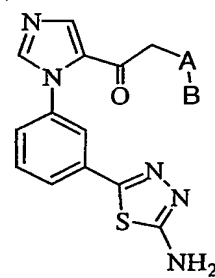
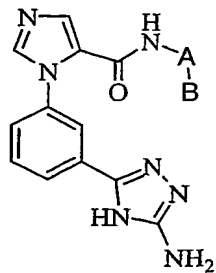
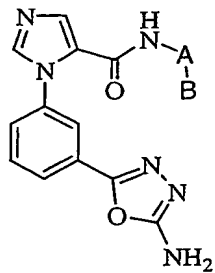
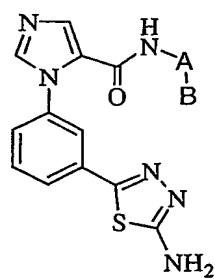
Examples -360 use the structures from Table 1 and the corresponding A and B groups from Examples -360 of Table 1, and:

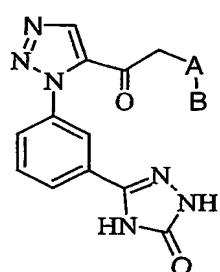
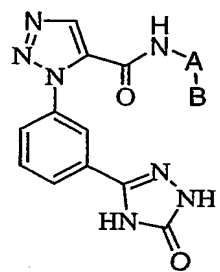
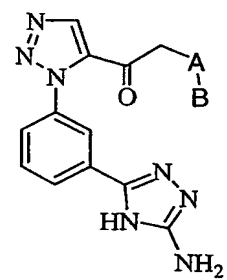
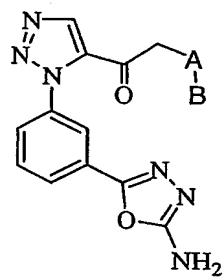
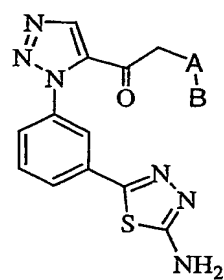
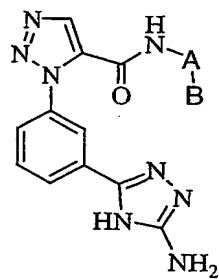
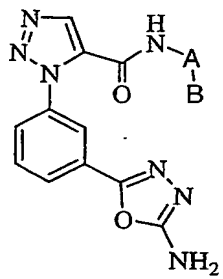
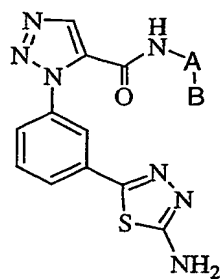
R<sup>1a</sup> is 1-tetrazolyl-CH<sub>2</sub>-.

20

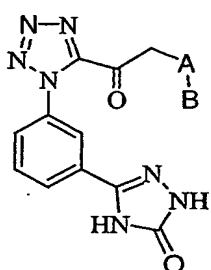
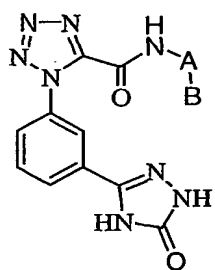
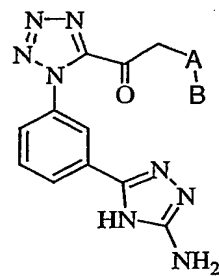
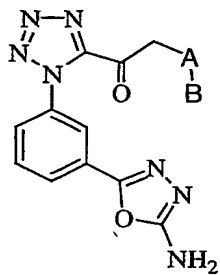
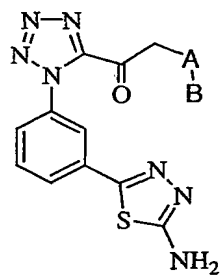
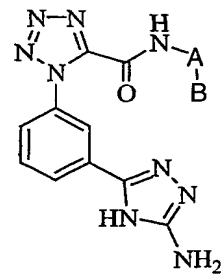
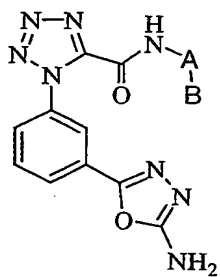
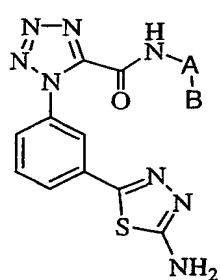
Table 17

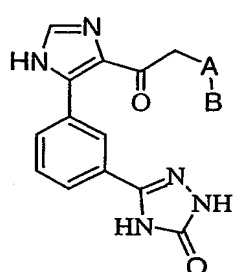
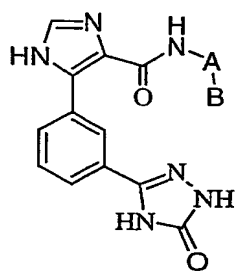
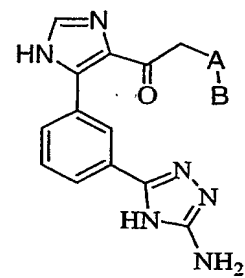
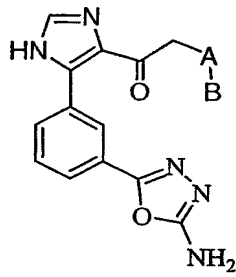
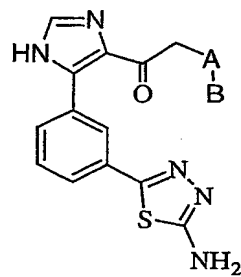
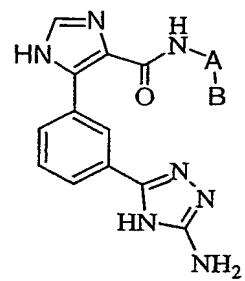
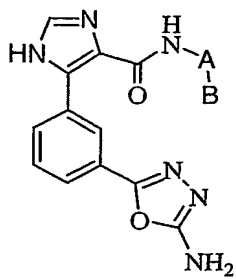
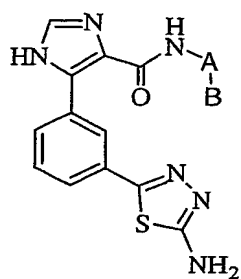


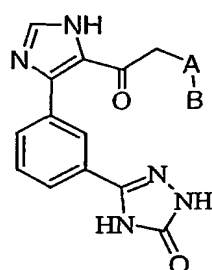
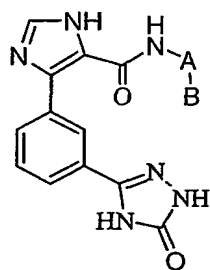
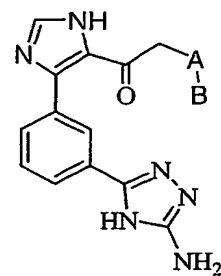
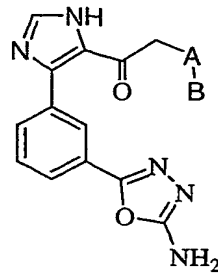
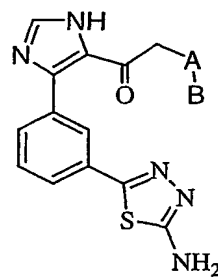
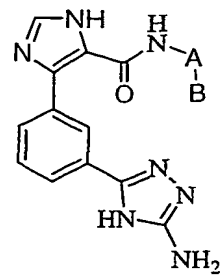
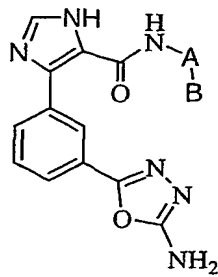
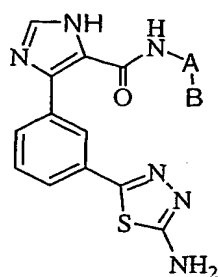


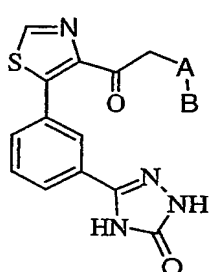
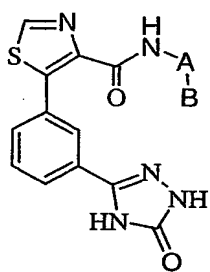
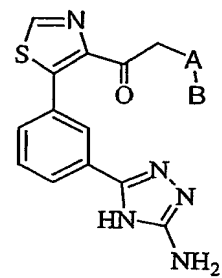
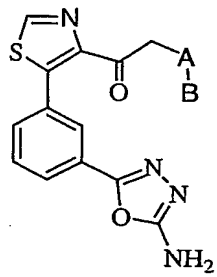
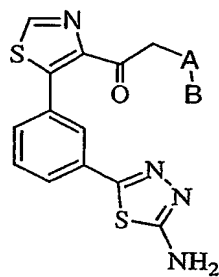
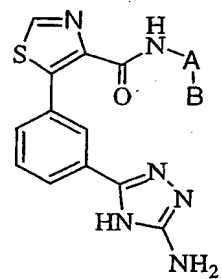
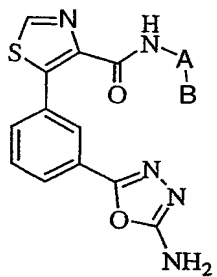
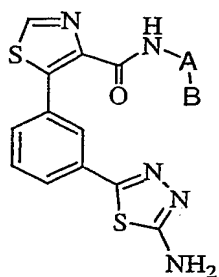


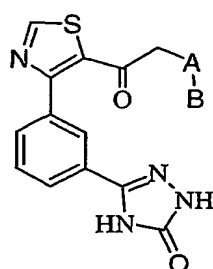
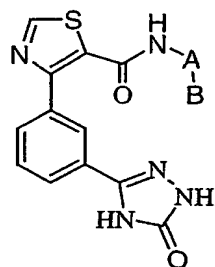
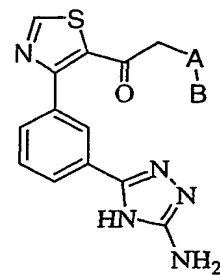
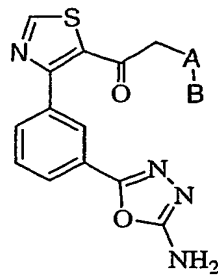
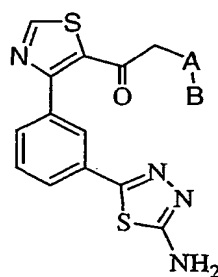
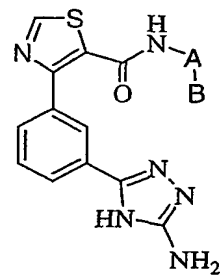
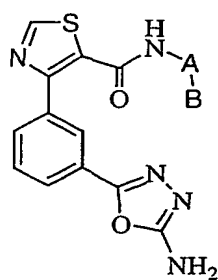
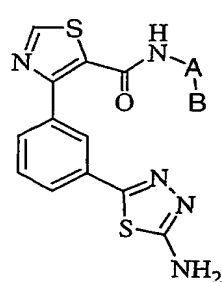












Ex#	A	B
5	1. phenyl	2-(NH <sub>2</sub> SO <sub>2</sub> )phenyl
	2. phenyl	2-(CH <sub>3</sub> SO <sub>2</sub> )phenyl
	3. phenyl	3-NH <sub>2</sub> SO <sub>2</sub> -4-pyridyl
	4. phenyl	3-CH <sub>3</sub> SO <sub>2</sub> -4-pyridyl
	5. phenyl	2-(CH <sub>3</sub> NH)phenyl
	6. phenyl	3-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-4-pyridyl
10	7. phenyl	2-(N-(3-R-HO-pyrrolidinyl)CH <sub>2</sub> )phenyl
	8. phenyl	2-(N-(4-HO-piperidinyl)CH <sub>2</sub> )phenyl
	9. phenyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
15	10. phenyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )phenyl
	11. phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )phenyl
	12. phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
	13. phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )phenyl
	14. phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )phenyl
	15. phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )phenyl
20	16. phenyl	2-((cyclopropyl)NHCH <sub>2</sub> )phenyl
	17. phenyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	18. phenyl	2-((cyclobutyl)NHCH <sub>2</sub> )phenyl
	19. phenyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	20. phenyl	2-((cyclopentyl)NHCH <sub>2</sub> )phenyl
	21. phenyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )phenyl

	22.	phenyl	2-((cyclohexyl)NHCH <sub>2</sub> )phenyl
	23.	phenyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	24.	phenyl	1-CH <sub>3</sub> -2-imidazolyl
	25.	phenyl	2-CH <sub>3</sub> -1-imidazolyl
5	26.	phenyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	27.	phenyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	28.	phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	29.	phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	30.	phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )-1-imidazolyl
10	31.	phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )-1-imidazolyl
	32.	phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	33.	phenyl	2-((cyclopropyl)NHCH <sub>2</sub> )-1-imidazolyl
	34.	phenyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	35.	phenyl	2-((cyclobutyl)NHCH <sub>2</sub> )-1-imidazolyl
15	36.	phenyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	37.	phenyl	2-((cyclopentyl)NHCH <sub>2</sub> )-1-imidazolyl
	38.	phenyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	39.	phenyl	2-((cyclohexyl)NHCH <sub>2</sub> )-1-imidazolyl
	40.	phenyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
20	41.	2-pyridyl	2-(NH <sub>2</sub> SO <sub>2</sub> )phenyl
	42.	2-pyridyl	2-(CH <sub>3</sub> SO <sub>2</sub> )phenyl
	43.	2-pyridyl	3-NH <sub>2</sub> SO <sub>2</sub> -4-pyridyl
	44.	2-pyridyl	3-CH <sub>3</sub> SO <sub>2</sub> -4-pyridyl
	45.	2-pyridyl	2-(CH <sub>3</sub> NH)phenyl
25	46.	2-pyridyl	3-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-4-pyridyl
	47.	2-pyridyl	2-(N-(3-R-HO-pyrrolidinyl)CH <sub>2</sub> )phenyl
	48.	2-pyridyl	2-(N-(4-HO-piperidinyl)CH <sub>2</sub> )phenyl
	49.	2-pyridyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
	50.	2-pyridyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )phenyl
30	51.	2-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )phenyl
	52.	2-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
	53.	2-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )phenyl
	54.	2-pyridyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )phenyl
	55.	2-pyridyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )phenyl
35	56.	2-pyridyl	2-((cyclopropyl)NHCH <sub>2</sub> )phenyl
	57.	2-pyridyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	58.	2-pyridyl	2-((cyclobutyl)NHCH <sub>2</sub> )phenyl
	59.	2-pyridyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	60.	2-pyridyl	2-((cyclopentyl)NHCH <sub>2</sub> )phenyl
40	61.	2-pyridyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	62.	2-pyridyl	2-((cyclohexyl)NHCH <sub>2</sub> )phenyl
	63.	2-pyridyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	64.	2-pyridyl	1-CH <sub>3</sub> -2-imidazolyl
	65.	2-pyridyl	2-CH <sub>3</sub> -1-imidazolyl
45	66.	2-pyridyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	67.	2-pyridyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	68.	2-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	69.	2-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	70.	2-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )-1-imidazolyl
50	71.	2-pyridyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )-1-imidazolyl
	72.	2-pyridyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	73.	2-pyridyl	2-((cyclopropyl)NHCH <sub>2</sub> )-1-imidazolyl
	74.	2-pyridyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl

	75.	2-pyridyl	2-((cyclobutyl)NHCH <sub>2</sub> )-1-imidazolyl
	76.	2-pyridyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	77.	2-pyridyl	2-((cyclopentyl)NHCH <sub>2</sub> )-1-imidazolyl
	78.	2-pyridyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
5	79.	2-pyridyl	2-((cyclohexyl)NHCH <sub>2</sub> )-1-imidazolyl
	80.	2-pyridyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	81.	3-pyridyl	2-(NH <sub>2</sub> SO <sub>2</sub> )phenyl
	82.	3-pyridyl	2-(CH <sub>3</sub> SO <sub>2</sub> )phenyl
	83.	3-pyridyl	3-NH <sub>2</sub> SO <sub>2</sub> -4-pyridyl
10	84.	3-pyridyl	3-CH <sub>3</sub> SO <sub>2</sub> -4-pyridyl
	85.	3-pyridyl	2-(CH <sub>3</sub> NH)phenyl
	86.	3-pyridyl	3-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-4-pyridyl
	87.	3-pyridyl	2-(N-(3-R-HO-pyrrolidinyl)CH <sub>2</sub> )phenyl
	88.	3-pyridyl	2-(N-(4-HO-piperidinyl)CH <sub>2</sub> )phenyl
15	89.	3-pyridyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
	90.	3-pyridyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )phenyl
	91.	3-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )phenyl
	92.	3-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
	93.	3-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )phenyl
20	94.	3-pyridyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )phenyl
	95.	3-pyridyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )phenyl
	96.	3-pyridyl	2-((cyclopropyl)NHCH <sub>2</sub> )phenyl
	97.	3-pyridyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	98.	3-pyridyl	2-((cyclobutyl)NHCH <sub>2</sub> )phenyl
25	99.	3-pyridyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	100.	3-pyridyl	2-((cyclopentyl)NHCH <sub>2</sub> )phenyl
	101.	3-pyridyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	102.	3-pyridyl	2-((cyclohexyl)NHCH <sub>2</sub> )phenyl
	103.	3-pyridyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
30	104.	3-pyridyl	1-CH <sub>3</sub> -2-imidazolyl
	105.	3-pyridyl	2-CH <sub>3</sub> -1-imidazolyl
	106.	3-pyridyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	107.	3-pyridyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	108.	3-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )-1-imidazolyl
35	109.	3-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	110.	3-pyridyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )-1-imidazolyl
	111.	3-pyridyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )-1-imidazolyl
	112.	3-pyridyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	113.	3-pyridyl	2-((cyclopropyl)NHCH <sub>2</sub> )-1-imidazolyl
40	114.	3-pyridyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	115.	3-pyridyl	2-((cyclobutyl)NHCH <sub>2</sub> )-1-imidazolyl
	116.	3-pyridyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	117.	3-pyridyl	2-((cyclopentyl)NHCH <sub>2</sub> )-1-imidazolyl
	118.	3-pyridyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
45	119.	3-pyridyl	2-((cyclohexyl)NHCH <sub>2</sub> )-1-imidazolyl
	120.	3-pyridyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	121.	2-pyrimidyl	2-(NH <sub>2</sub> SO <sub>2</sub> )phenyl
	122.	2-pyrimidyl	2-(CH <sub>3</sub> SO <sub>2</sub> )phenyl
	123.	2-pyrimidyl	3-NH <sub>2</sub> SO <sub>2</sub> -4-pyridyl
50	124.	2-pyrimidyl	3-CH <sub>3</sub> SO <sub>2</sub> -4-pyridyl
	125.	2-pyrimidyl	2-(CH <sub>3</sub> NH)phenyl
	126.	2-pyrimidyl	3-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-4-pyridyl
	127.	2-pyrimidyl	2-(N-(3-R-HO-pyrrolidinyl)CH <sub>2</sub> )phenyl

128. 2-pyrimidyl 2-(N-(4-HO-piperidinyl)CH<sub>2</sub>)phenyl
129. 2-pyrimidyl 2-((CH<sub>3</sub>)<sub>2</sub>NCH<sub>2</sub>)phenyl
130. 2-pyrimidyl 2-((CH<sub>3</sub>)NHCH<sub>2</sub>)phenyl
131. 2-pyrimidyl 2-((CH<sub>3</sub>CH<sub>2</sub>)NHCH<sub>2</sub>)phenyl
- 5 132. 2-pyrimidyl 2-((CH<sub>3</sub>CH<sub>2</sub>)<sub>2</sub>NCH<sub>2</sub>)phenyl
133. 2-pyrimidyl 2-((CH<sub>3</sub>CH<sub>2</sub>)N(CH<sub>3</sub>)CH<sub>2</sub>)phenyl
134. 2-pyrimidyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)NHCH<sub>2</sub>)phenyl
135. 2-pyrimidyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)<sub>2</sub>NCH<sub>2</sub>)phenyl
- 10 136. 2-pyrimidyl 2-((cyclopropyl)NHCH<sub>2</sub>)phenyl
137. 2-pyrimidyl 2-((cyclopropyl)<sub>2</sub>NCH<sub>2</sub>)phenyl
138. 2-pyrimidyl 2-((cyclobutyl)NHCH<sub>2</sub>)phenyl
139. 2-pyrimidyl 2-((cyclobutyl)<sub>2</sub>NCH<sub>2</sub>)phenyl
140. 2-pyrimidyl 2-((cyclopentyl)NHCH<sub>2</sub>)phenyl
141. 2-pyrimidyl 2-((cyclopentyl)<sub>2</sub>NCH<sub>2</sub>)phenyl
- 15 142. 2-pyrimidyl 2-((cyclohexyl)NHCH<sub>2</sub>)phenyl
143. 2-pyrimidyl 2-((cyclohexyl)<sub>2</sub>NCH<sub>2</sub>)phenyl
144. 2-pyrimidyl 1-CH<sub>3</sub>-2-imidazolyl
145. 2-pyrimidyl 2-CH<sub>3</sub>-1-imidazolyl
146. 2-pyrimidyl 2-((CH<sub>3</sub>)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl
- 20 147. 2-pyrimidyl 2-((CH<sub>3</sub>)NHCH<sub>2</sub>)-1-imidazolyl
148. 2-pyrimidyl 2-((CH<sub>3</sub>CH<sub>2</sub>)NHCH<sub>2</sub>)-1-imidazolyl
149. 2-pyrimidyl 2-((CH<sub>3</sub>CH<sub>2</sub>)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl
150. 2-pyrimidyl 2-((CH<sub>3</sub>CH<sub>2</sub>)N(CH<sub>3</sub>)CH<sub>2</sub>)-1-imidazolyl
151. 2-pyrimidyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)NHCH<sub>2</sub>)-1-imidazolyl
- 25 152. 2-pyrimidyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl
153. 2-pyrimidyl 2-((cyclopropyl)NHCH<sub>2</sub>)-1-imidazolyl
154. 2-pyrimidyl 2-((cyclopropyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl
155. 2-pyrimidyl 2-((cyclobutyl)NHCH<sub>2</sub>)-1-imidazolyl
156. 2-pyrimidyl 2-((cyclobutyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl
- 30 157. 2-pyrimidyl 2-((cyclopentyl)NHCH<sub>2</sub>)-1-imidazolyl
158. 2-pyrimidyl 2-((cyclopentyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl
159. 2-pyrimidyl 2-((cyclohexyl)NHCH<sub>2</sub>)-1-imidazolyl
160. 2-pyrimidyl 2-((cyclohexyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl
161. 5-pyrimidyl 2-(NH<sub>2</sub>SO<sub>2</sub>)phenyl
- 35 162. 5-pyrimidyl 2-(CH<sub>3</sub>SO<sub>2</sub>)phenyl
163. 5-pyrimidyl 3-NH<sub>2</sub>SO<sub>2</sub>-4-pyridyl
164. 5-pyrimidyl 3-CH<sub>3</sub>SO<sub>2</sub>-4-pyridyl
165. 5-pyrimidyl 2-(CH<sub>3</sub>NH)phenyl
166. 5-pyrimidyl 3-((CH<sub>3</sub>)<sub>2</sub>NCH<sub>2</sub>)-4-pyridyl
- 40 167. 5-pyrimidyl 2-(N-(3-R-HO-pyrrolidinyl)CH<sub>2</sub>)phenyl
168. 5-pyrimidyl 2-(N-(4-HO-piperidinyl)CH<sub>2</sub>)phenyl
169. 5-pyrimidyl 2-((CH<sub>3</sub>)<sub>2</sub>NCH<sub>2</sub>)phenyl
170. 5-pyrimidyl 2-((CH<sub>3</sub>)NHCH<sub>2</sub>)phenyl
171. 5-pyrimidyl 2-((CH<sub>3</sub>CH<sub>2</sub>)NHCH<sub>2</sub>)phenyl
- 45 172. 5-pyrimidyl 2-((CH<sub>3</sub>CH<sub>2</sub>)<sub>2</sub>NCH<sub>2</sub>)phenyl
173. 5-pyrimidyl 2-((CH<sub>3</sub>CH<sub>2</sub>)N(CH<sub>3</sub>)CH<sub>2</sub>)phenyl
174. 5-pyrimidyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)NHCH<sub>2</sub>)phenyl
175. 5-pyrimidyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)<sub>2</sub>NCH<sub>2</sub>)phenyl
176. 5-pyrimidyl 2-((cyclopropyl)NHCH<sub>2</sub>)phenyl
- 50 177. 5-pyrimidyl 2-((cyclopropyl)<sub>2</sub>NCH<sub>2</sub>)phenyl
178. 5-pyrimidyl 2-((cyclobutyl)NHCH<sub>2</sub>)phenyl
179. 5-pyrimidyl 2-((cyclobutyl)<sub>2</sub>NCH<sub>2</sub>)phenyl
180. 5-pyrimidyl 2-((cyclopentyl)NHCH<sub>2</sub>)phenyl



	181.	5-pyrimidyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	182.	5-pyrimidyl	2-((cyclohexyl)NHCH <sub>2</sub> )phenyl
	183.	5-pyrimidyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	184.	5-pyrimidyl	1-CH <sub>3</sub> -2-imidazolyl
5	185.	5-pyrimidyl	2-CH <sub>3</sub> -1-imidazolyl
	186.	5-pyrimidyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	187.	5-pyrimidyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	188.	5-pyrimidyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	189.	5-pyrimidyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
10	190.	5-pyrimidyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )-1-imidazolyl
	191.	5-pyrimidyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )-1-imidazolyl
	192.	5-pyrimidyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	193.	5-pyrimidyl	2-((cyclopropyl)NHCH <sub>2</sub> )-1-imidazolyl
	194.	5-pyrimidyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
15	195.	5-pyrimidyl	2-((cyclobutyl)NHCH <sub>2</sub> )-1-imidazolyl
	196.	5-pyrimidyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	197.	5-pyrimidyl	2-((cyclopentyl)NHCH <sub>2</sub> )-1-imidazolyl
	198.	5-pyrimidyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	199.	5-pyrimidyl	2-((cyclohexyl)NHCH <sub>2</sub> )-1-imidazolyl
20	200.	5-pyrimidyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	201.	2-Cl-phenyl	2-(NH <sub>2</sub> SO <sub>2</sub> )phenyl
	202.	2-Cl-phenyl	2-(CH <sub>3</sub> SO <sub>2</sub> )phenyl
	203.	2-Cl-phenyl	3-NH <sub>2</sub> SO <sub>2</sub> -4-pyridyl
	204.	2-Cl-phenyl	3-CH <sub>3</sub> SO <sub>2</sub> -4-pyridyl
25	205.	2-Cl-phenyl	2-(CH <sub>3</sub> NH)phenyl
	206.	2-Cl-phenyl	3-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-4-pyridyl
	207.	2-Cl-phenyl	2-(N-(3-R-HO-pyrrolidinyl)CH <sub>2</sub> )phenyl
	208.	2-Cl-phenyl	2-(N-(4-HO-piperidinyl)CH <sub>2</sub> )phenyl
	209.	2-Cl-phenyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
30	210.	2-Cl-phenyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )phenyl
	211.	2-Cl-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )phenyl
	212.	2-Cl-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
	213.	2-Cl-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )phenyl
	214.	2-Cl-phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )phenyl
35	215.	2-Cl-phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )phenyl
	216.	2-Cl-phenyl	2-((cyclopropyl)NHCH <sub>2</sub> )phenyl
	217.	2-Cl-phenyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	218.	2-Cl-phenyl	2-((cyclobutyl)NHCH <sub>2</sub> )phenyl
	219.	2-Cl-phenyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
40	220.	2-Cl-phenyl	2-((cyclopentyl)NHCH <sub>2</sub> )phenyl
	221.	2-Cl-phenyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	222.	2-Cl-phenyl	2-((cyclohexyl)NHCH <sub>2</sub> )phenyl
	223.	2-Cl-phenyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	224.	2-Cl-phenyl	1-CH <sub>3</sub> -2-imidazolyl
45	225.	2-Cl-phenyl	2-CH <sub>3</sub> -1-imidazolyl
	226.	2-Cl-phenyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	227.	2-Cl-phenyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	228.	2-Cl-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	229.	2-Cl-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
50	230.	2-Cl-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )-1-imidazolyl
	231.	2-Cl-phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )-1-imidazolyl
	232.	2-Cl-phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	233.	2-Cl-phenyl	2-((cyclopropyl)NHCH <sub>2</sub> )-1-imidazolyl

	234.	2-Cl-phenyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	235.	2-Cl-phenyl	2-((cyclobutyl)NHCH <sub>2</sub> )-1-imidazolyl
	236.	2-Cl-phenyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
5	237.	2-Cl-phenyl	2-((cyclopentyl)NHCH <sub>2</sub> )-1-imidazolyl
	238.	2-Cl-phenyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	239.	2-Cl-phenyl	2-((cyclohexyl)NHCH <sub>2</sub> )-1-imidazolyl
	240.	2-Cl-phenyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	241.	2-F-phenyl	2-(NH <sub>2</sub> SO <sub>2</sub> )phenyl
10	242.	2-F-phenyl	2-(CH <sub>3</sub> SO <sub>2</sub> )phenyl
	243.	2-F-phenyl	3-NH <sub>2</sub> SO <sub>2</sub> -4-pyridyl
	244.	2-F-phenyl	3-CH <sub>3</sub> SO <sub>2</sub> -4-pyridyl
	245.	2-F-phenyl	2-(CH <sub>3</sub> NH)phenyl
	246.	2-F-phenyl	3-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-4-pyridyl
15	247.	2-F-phenyl	2-(N-(3-R-HO-pyrrolidinyl)CH <sub>2</sub> )phenyl
	248.	2-F-phenyl	2-(N-(4-HO-piperidinyl)CH <sub>2</sub> )phenyl
	249.	2-F-phenyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
	250.	2-F-phenyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )phenyl
	251.	2-F-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )phenyl
20	252.	2-F-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
	253.	2-F-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )phenyl
	254.	2-F-phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )phenyl
	255.	2-F-phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )phenyl
	256.	2-F-phenyl	2-((cyclopropyl)NHCH <sub>2</sub> )phenyl
25	257.	2-F-phenyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	258.	2-F-phenyl	2-((cyclobutyl)NHCH <sub>2</sub> )phenyl
	259.	2-F-phenyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	260.	2-F-phenyl	2-((cyclopentyl)NHCH <sub>2</sub> )phenyl
	261.	2-F-phenyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
30	262.	2-F-phenyl	2-((cyclohexyl)NHCH <sub>2</sub> )phenyl
	263.	2-F-phenyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	264.	2-F-phenyl	1-CH <sub>3</sub> -2-imidazolyl
	265.	2-F-phenyl	2-CH <sub>3</sub> -1-imidazolyl
	266.	2-F-phenyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
35	267.	2-F-phenyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	268.	2-F-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	269.	2-F-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	270.	2-F-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )-1-imidazolyl
	271.	2-F-phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )-1-imidazolyl
40	272.	2-F-phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	273.	2-F-phenyl	2-((cyclopropyl)NHCH <sub>2</sub> )-1-imidazolyl
	274.	2-F-phenyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	275.	2-F-phenyl	2-((cyclobutyl)NHCH <sub>2</sub> )-1-imidazolyl
	276.	2-F-phenyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
45	277.	2-F-phenyl	2-((cyclopentyl)NHCH <sub>2</sub> )-1-imidazolyl
	278.	2-F-phenyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	279.	2-F-phenyl	2-((cyclohexyl)NHCH <sub>2</sub> )-1-imidazolyl
	280.	2-F-phenyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	281.	2,6-diF-phenyl	2-(NH <sub>2</sub> SO <sub>2</sub> )phenyl
50	282.	2,6-diF-phenyl	2-(CH <sub>3</sub> SO <sub>2</sub> )phenyl
	283.	2,6-diF-phenyl	3-NH <sub>2</sub> SO <sub>2</sub> -4-pyridyl
	284.	2,6-diF-phenyl	3-CH <sub>3</sub> SO <sub>2</sub> -4-pyridyl
	285.	2,6-diF-phenyl	2-(CH <sub>3</sub> NH)phenyl
	286.	2,6-diF-phenyl	3-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-4-pyridyl

	287. 2,6-diF-phenyl	2-(N-(3-R-HO-pyrrolidinyl)CH <sub>2</sub> )phenyl
	288. 2,6-diF-phenyl	2-(N-(4-HO-piperidinyl)CH <sub>2</sub> )phenyl
	289. 2,6-diF-phenyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
	290. 2,6-diF-phenyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )phenyl
5	291. 2,6-diF-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )phenyl
	292. 2,6-diF-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
	293. 2,6-diF-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )phenyl
	294. 2,6-diF-phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )phenyl
	295. 2,6-diF-phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )phenyl
10	296. 2,6-diF-phenyl	2-((cyclopropyl)NHCH <sub>2</sub> )phenyl
	297. 2,6-diF-phenyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	298. 2,6-diF-phenyl	2-((cyclobutyl)NHCH <sub>2</sub> )phenyl
	299. 2,6-diF-phenyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	300. 2,6-diF-phenyl	2-((cyclopentyl)NHCH <sub>2</sub> )phenyl
15	301. 2,6-diF-phenyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	302. 2,6-diF-phenyl	2-((cyclohexyl)NHCH <sub>2</sub> )phenyl
	303. 2,6-diF-phenyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	304. 2,6-diF-phenyl	1-CH <sub>3</sub> -2-imidazolyl
	305. 2,6-diF-phenyl	2-CH <sub>3</sub> -1-imidazolyl
20	306. 2,6-diF-phenyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	307. 2,6-diF-phenyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	308. 2,6-diF-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )-1-imidazolyl
	309. 2,6-diF-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	310. 2,6-diF-phenyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )-1-imidazolyl
25	311. 2,6-diF-phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )-1-imidazolyl
	312. 2,6-diF-phenyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	313. 2,6-diF-phenyl	2-((cyclopropyl)NHCH <sub>2</sub> )-1-imidazolyl
	314. 2,6-diF-phenyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	315. 2,6-diF-phenyl	2-((cyclobutyl)NHCH <sub>2</sub> )-1-imidazolyl
30	316. 2,6-diF-phenyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	317. 2,6-diF-phenyl	2-((cyclopentyl)NHCH <sub>2</sub> )-1-imidazolyl
	318. 2,6-diF-phenyl	2-((cyclopentyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
	319. 2,6-diF-phenyl	2-((cyclohexyl)NHCH <sub>2</sub> )-1-imidazolyl
	320. 2,6-diF-phenyl	2-((cyclohexyl) <sub>2</sub> NCH <sub>2</sub> )-1-imidazolyl
35	321. piperidinyl	2-(NH <sub>2</sub> SO <sub>2</sub> )phenyl
	322. piperidinyl	2-(CH <sub>3</sub> SO <sub>2</sub> )phenyl
	323. piperidinyl	3-NH <sub>2</sub> SO <sub>2</sub> -4-pyridyl
	324. piperidinyl	3-CH <sub>3</sub> SO <sub>2</sub> -4-pyridyl
	325. piperidinyl	2-(CH <sub>3</sub> NH)phenyl
40	326. piperidinyl	3-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )-4-pyridyl
	327. piperidinyl	2-(N-(3-R-HO-pyrrolidinyl)CH <sub>2</sub> )phenyl
	328. piperidinyl	2-(N-(4-HO-piperidinyl)CH <sub>2</sub> )phenyl
	329. piperidinyl	2-((CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
	330. piperidinyl	2-((CH <sub>3</sub> )NHCH <sub>2</sub> )phenyl
45	331. piperidinyl	2-((CH <sub>3</sub> CH <sub>2</sub> )NHCH <sub>2</sub> )phenyl
	332. piperidinyl	2-((CH <sub>3</sub> CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> )phenyl
	333. piperidinyl	2-((CH <sub>3</sub> CH <sub>2</sub> )N(CH <sub>3</sub> )CH <sub>2</sub> )phenyl
	334. piperidinyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH)NHCH <sub>2</sub> )phenyl
	335. piperidinyl	2-(((CH <sub>3</sub> ) <sub>2</sub> CH) <sub>2</sub> NCH <sub>2</sub> )phenyl
50	336. piperidinyl	2-((cyclopropyl)NHCH <sub>2</sub> )phenyl
	337. piperidinyl	2-((cyclopropyl) <sub>2</sub> NCH <sub>2</sub> )phenyl
	338. piperidinyl	2-((cyclobutyl)NHCH <sub>2</sub> )phenyl
	339. piperidinyl	2-((cyclobutyl) <sub>2</sub> NCH <sub>2</sub> )phenyl

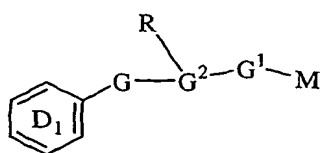
340. piperidinyl 2-((cyclopentyl)NHCH<sub>2</sub>)phenyl  
341. piperidinyl 2-((cyclopentyl)<sub>2</sub>NCH<sub>2</sub>)phenyl  
342. piperidinyl 2-((cyclohexyl)NHCH<sub>2</sub>)phenyl  
343. piperidinyl 2-((cyclohexyl)<sub>2</sub>NCH<sub>2</sub>)phenyl  
5 344. piperidinyl 1-CH<sub>3</sub>-2-imidazolyl  
345. piperidinyl 2-CH<sub>3</sub>-1-imidazolyl  
346. piperidinyl 2-((CH<sub>3</sub>)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
347. piperidinyl 2-((CH<sub>3</sub>)NHCH<sub>2</sub>)-1-imidazolyl  
348. piperidinyl 2-((CH<sub>3</sub>CH<sub>2</sub>)NHCH<sub>2</sub>)-1-imidazolyl  
10 349. piperidinyl 2-((CH<sub>3</sub>CH<sub>2</sub>)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
350. piperidinyl 2-((CH<sub>3</sub>CH<sub>2</sub>)N(CH<sub>3</sub>)CH<sub>2</sub>)-1-imidazolyl  
351. piperidinyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)NHCH<sub>2</sub>)-1-imidazolyl  
352. piperidinyl 2-(((CH<sub>3</sub>)<sub>2</sub>CH)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
353. piperidinyl 2-((cyclopropyl)NHCH<sub>2</sub>)-1-imidazolyl  
15 354. piperidinyl 2-((cyclopropyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
355. piperidinyl 2-((cyclobutyl)NHCH<sub>2</sub>)-1-imidazolyl  
356. piperidinyl 2-((cyclobutyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
357. piperidinyl 2-((cyclopentyl)NHCH<sub>2</sub>)-1-imidazolyl  
358. piperidinyl 2-((cyclopentyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl  
20 359. piperidinyl 2-((cyclohexyl)NHCH<sub>2</sub>)-1-imidazolyl  
360. piperidinyl 2-((cyclohexyl)<sub>2</sub>NCH<sub>2</sub>)-1-imidazolyl

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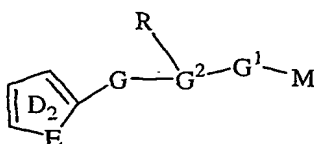
Numerous modifications and variations of the present invention are possible in light of the above teachings. It is therefore to be understood that within the scope of the appended claims, the invention may be practiced  
30 otherwise that as specifically described herein.

WHAT IS CLAIMED IS:

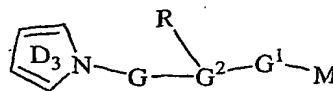
1. A compound of formula Ia, Ib, or Ic:



Ia



Ib



Ic

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

ring D<sub>1</sub> is selected from pyridine, pyrazine, pyridazine, and pyrimidine and is substituted with 1 R<sup>a</sup> and 0-1 R<sup>b</sup>;

ring D<sub>2</sub> is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-3 N atoms, wherein E is selected from O, S, and N-R<sup>c</sup> and ring D<sub>2</sub> is substituted with 1 R<sup>a</sup> and 0-1 R<sup>b</sup>;

ring D<sub>3</sub> is a 5-membered heteroaromatic ring system comprising carbon atoms and from 0-3 additional N atoms and ring D<sub>3</sub> is substituted with 1 R<sup>a</sup> and 0-1 R<sup>b</sup>;

R is selected from H, C<sub>1-4</sub> alkyl, F, Cl, Br, I, OH, OCH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>, OCH(CH<sub>3</sub>)<sub>2</sub>, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CN, C(=NR<sup>8</sup>)NR<sup>7</sup>R<sup>9</sup>, NHC(=NR<sup>8</sup>)NR<sup>7</sup>R<sup>9</sup>, NR<sup>8</sup>CH(=NR<sup>7</sup>), NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, C(=NH)NH<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>NR<sup>7</sup>R<sup>8</sup>, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>C(O)NR<sup>7</sup>R<sup>8</sup>, and OCF<sub>3</sub>;

R<sup>a</sup> is selected from H, C<sub>1-4</sub> alkyl, F, Cl, Br, I, OH, OCH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>, OCH(CH<sub>3</sub>)<sub>2</sub>, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CN, C(=NR<sup>8</sup>)NR<sup>7</sup>R<sup>9</sup>, NHC(=NR<sup>8</sup>)NR<sup>7</sup>R<sup>9</sup>, NR<sup>8</sup>CH(=NR<sup>7</sup>), NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub>

alkyl)<sub>2</sub>, C(=NH)NH<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>NR<sup>7</sup>R<sup>8</sup>, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>C(O)NR<sup>7</sup>R<sup>8</sup>, and OCF<sub>3</sub>;

5 R<sup>b</sup> is selected from H, C<sub>1-4</sub> alkyl, F, Cl, Br, I, OH, OCH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>, OCH(CH<sub>3</sub>)<sub>2</sub>, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CN, C(=NR<sup>8</sup>)NR<sup>7</sup>R<sup>9</sup>, NHC(=NR<sup>8</sup>)NR<sup>7</sup>R<sup>9</sup>, NR<sup>8</sup>CH(=NR<sup>7</sup>), NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, C(=NH)NH<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>NR<sup>7</sup>R<sup>8</sup>, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>C(O)NR<sup>7</sup>R<sup>8</sup>, and OCF<sub>3</sub>;

R<sup>c</sup> is selected from H, C<sub>1-4</sub> alkyl, OCH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>, OCH(CH<sub>3</sub>)<sub>2</sub>, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, C(=NH)NH<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>NR<sup>7</sup>R<sup>8</sup>, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>C(O)NR<sup>7</sup>R<sup>8</sup>, and OCF<sub>3</sub>;

G is absent or is selected from CH<sub>2</sub>, C(O), O, NR<sup>3</sup>, S(O)<sub>p</sub>, CH<sub>2</sub>CH<sub>2</sub>, C(O)CH<sub>2</sub>, CH<sub>2</sub>C(O), OCH<sub>2</sub>, CH<sub>2</sub>O, NR<sup>3</sup>CH<sub>2</sub>, CH<sub>2</sub>NR<sup>3</sup>, S(O)<sub>p</sub>CH<sub>2</sub>, CH<sub>2</sub>S(O)<sub>p</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>, C(O)CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>C(O)CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>C(O), OCH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>OCH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>O, NR<sup>3</sup>CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>NR<sup>3</sup>CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NR<sup>3</sup>, S(O)<sub>p</sub>CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>S(O)<sub>p</sub>CH<sub>2</sub>, and CH<sub>2</sub>CH<sub>2</sub>S(O)<sub>p</sub>;

G<sub>1</sub> is absent or is selected from (CR<sup>3</sup>R<sup>3a</sup>)<sub>1-5</sub>,  
 25 (CR<sup>3</sup>R<sup>3a</sup>)<sub>0-2</sub>CR<sup>3</sup>=CR<sup>3</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>0-2</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>0-2</sub>C≡C(CR<sup>3</sup>R<sup>3a</sup>)<sub>0-2</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>C(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>C(O)O(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>OC(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>O(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>C(O)NR<sup>3</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3</sup>C(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>OC(O)NR<sup>3</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 30 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3</sup>C(O)O(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3</sup>C(O)NR<sup>3</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3</sup>C(S)NR<sup>3</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(O)<sub>2</sub>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(O)NR<sup>3</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3</sup>S(O)<sub>2</sub>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(O)<sub>2</sub>NR<sup>3</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, and (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3</sup>S(O)<sub>2</sub>NR<sup>3</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>.

wherein  $u + w$  total 0, 1, 2, 3, or 4, provided that  $G_1$  does not form a N-N, N-O, N-S,  $NCH_2N$ ,  $NCH_2O$ , or  $NCH_2S$  bond with either group to which it is attached;

- 5  $G^2$  is phenyl, naphthyl, or a 5-10 membered heteroaryl consisting of carbon atoms and from 1-3 heteroatoms selected from N, O, and S;

- 10 M is isoxazoline, pyrazoline, isothiazoline, triazoline, tetrazoline, phenyl, or a 5-6 membered aromatic heterocycle consisting of carbon atoms and 1-4 heteroatoms selected from O, N, and S, and is substituted with -Z-A-B;

- 15 M is also substituted with 0-2  $R^{1a}$ ;

- Z is selected from a bond,  $-(CR^2R^{2a})_{1-4}-$ ,  $(CR^2R^{2a})_qO(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qNR^3(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qC(O)(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qC(O)O(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qOC(O)(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qC(O)NR^3(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qNR^3C(O)(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qOC(O)O(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qOC(O)NR^3(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qNR^3C(O)O(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qNR^3C(O)NR^3(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qS(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qS(O)(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qS(O)_2(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qSO_2NR^3(CR^2R^{2a})_{q^1}$ ,  $(CR^2R^{2a})_qNR^3SO_2(CR^2R^{2a})_{q^1}$ , and  $(CR^2R^{2a})_qNR^3SO_2NR^3(CR^2R^{2a})_{q^1}$ ,  
 20 wherein  $q + q^1$  total 0, 1, or 2, provided that Z does not form a N-N, N-O, N-S,  $NCH_2N$ ,  $NCH_2O$ , or  $NCH_2S$  bond with either group to which it is attached;

- 30  $R^{1a}$  is selected from H,  $-(CH_2)_r-R^{1b}$ ,  $-CH=CH-R^{1b}$ ,  $NCH_2R^{1c}$ ,  $OCH_2R^{1c}$ ,  $SCH_2R^{1c}$ ,  $NH(CH_2)_2(CH_2)_tR^{1b}$ ,  $O(CH_2)_2(CH_2)_tR^{1b}$ ,  $S(CH_2)_2(CH_2)_tR^{1b}$ ,  $S(O)_p(CH_2)_rR^{1d}$ ,  $O(CH_2)_rR^{1d}$ ,  $NR^3(CH_2)_rR^{1d}$ ,  $OC(O)NR^3(CH_2)_rR^{1d}$ ,  $NR^3C(O)NR^3(CH_2)_rR^{1d}$ ,  $NR^3C(O)O(CH_2)_rR^{1d}$ ,

and  $\text{NR}^3\text{C}(\text{O})(\text{CH}_2)_r\text{R}^{1d}$ , provided that  $\text{R}^{1a}$  forms other than an N-halo, N-N, N-S, N-O, or N-CN bond;

alternatively, when two  $\text{R}^{1a}$ 's are attached to adjacent atoms, together with the atoms to which they are attached they form a 5-7 membered ring consisting of: carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and  $\text{S}(\text{O})_p$ , this ring being substituted with 0-2  $\text{R}^{4b}$  and comprising: 0-3 double bonds;

$\text{R}^{1b}$  is selected from H,  $\text{C}_{1-3}$  alkyl, F, Cl, Br, I, -CN, -CHO,  $(\text{CF}_2)_r\text{CF}_3$ ,  $(\text{CH}_2)_r\text{OR}^2$ ,  $\text{NR}^2\text{R}^{2a}$ ,  $\text{C}(\text{O})\text{R}^{2c}$ ,  $\text{OC}(\text{O})\text{R}^2$ ,  $(\text{CF}_2)_r\text{CO}_2\text{R}^{2a}$ ,  $\text{S}(\text{O})_p\text{R}^{2b}$ ,  $\text{NR}^2(\text{CH}_2)_r\text{OR}^2$ ,  $\text{C}(=\text{NR}^{2c})\text{NR}^2\text{R}^{2a}$ ,  $\text{NR}^2\text{C}(\text{O})\text{R}^{2b}$ ,  $\text{NR}^2\text{C}(\text{O})\text{NHR}^{2b}$ ,  $\text{NR}^2\text{C}(\text{O})_2\text{R}^{2a}$ ,  $\text{OC}(\text{O})\text{NR}^{2a}\text{R}^{2b}$ ,  $\text{C}(\text{O})\text{NR}^2\text{R}^{2a}$ ,  $\text{C}(\text{O})\text{NR}^2(\text{CH}_2)_r\text{OR}^2$ ,  $\text{SO}_2\text{NR}^2\text{R}^{2a}$ ,  $\text{NR}^2\text{SO}_2\text{R}^{2b}$ ,  $\text{C}_{3-6}$  carbocycle substituted with 0-2  $\text{R}^{4a}$ , and 5-10 membered heterocycle consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and  $\text{S}(\text{O})_p$  substituted with 0-2  $\text{R}^{4a}$ , provided that  $\text{R}^{1b}$  forms other than an N-halo, N-N, N-S, N-O, or N-CN bond;

$\text{R}^{1c}$  is selected from H,  $\text{CH}(\text{CH}_2\text{OR}^2)_2$ ,  $\text{C}(\text{O})\text{R}^{2c}$ ,  $\text{C}(\text{O})\text{NR}^2\text{R}^{2a}$ ,  $\text{S}(\text{O})\text{R}^{2b}$ ,  $\text{S}(\text{O})_2\text{R}^{2b}$ , and  $\text{SO}_2\text{NR}^2\text{R}^{2a}$ ;

$\text{R}^{1d}$  is selected from  $\text{C}_{3-13}$  carbocycle substituted with 0-2  $\text{R}^{4a}$ , and 5-13 membered heterocycle consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and  $\text{S}(\text{O})_p$  substituted with 0-2  $\text{R}^{4a}$ , provided that  $\text{R}^{1d}$  forms other than an N-N, N-S, or N-O bond;

$\text{R}^2$ , at each occurrence, is selected from H,  $\text{CF}_3$ ,  $\text{C}_{1-6}$  alkyl, benzyl,  $\text{C}_{3-6}$  carbocyclic residue substituted with 0-2



R<sup>4b</sup>, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R<sup>4b</sup>;

5

R<sup>2a</sup>, at each occurrence, is selected from H, CF<sub>3</sub>, C<sub>1-6</sub> alkyl, benzyl, phenethyl, C<sub>3-6</sub> carbocyclic residue substituted with 0-2 R<sup>4b</sup>, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R<sup>4b</sup>;

10

R<sup>2b</sup>, at each occurrence, is selected from CF<sub>3</sub>, C<sub>1-4</sub> alkoxy, C<sub>1-6</sub> alkyl, benzyl, C<sub>3-6</sub> carbocyclic residue substituted with 0-2 R<sup>4b</sup>, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R<sup>4b</sup>;

15

R<sup>2c</sup>, at each occurrence, is selected from CF<sub>3</sub>, OH, C<sub>1-4</sub> alkoxy, C<sub>1-6</sub> alkyl, benzyl, C<sub>3-6</sub> carbocyclic residue substituted with 0-2 R<sup>4b</sup>, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R<sup>4b</sup>;

20

25

alternatively, R<sup>2</sup> and R<sup>2a</sup>, together with the atom to which they are attached, combine to form a 5 or 6 membered saturated, partially saturated or unsaturated ring substituted with 0-2 R<sup>4b</sup> and comprising carbon atoms and from 0-1 additional heteroatoms selected from the group consisting of N, O, and S;

30

$R^3$ , at each occurrence, is selected from H,  $C_{1-4}$  alkyl, and phenyl;

$R^{3a}$ , at each occurrence, is selected from H,  $C_{1-4}$  alkyl, and phenyl;

$R^{3b}$ , at each occurrence, is selected from H,  $C_{1-4}$  alkyl, and phenyl;

$R^{3c}$ , at each occurrence, is selected from  $C_{1-4}$  alkyl, and phenyl;

$R^{3d}$ , at each occurrence, is selected from H,  $C_{1-4}$  alkyl,  $C_{1-4}$  alkyl-phenyl, and  $C(=O)R^{3c}$ ;

A is selected from:

$C_{3-10}$  carbocyclic residue substituted with 0-2  $R^4$ , and 5-12 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2  $R^4$ ;

B is selected from: H, Y, and X-Y, provided that Z and B -are attached to different atoms on A;

X is selected from  $-(CR^2R^{2a})_{1-4}-$ ,  $-CR^2(CR^2R^{2b})(CH_2)_t-$ ,  $-C(O)-$ ,  $-C(=NR^{1c})-$ ,  $-CR^2(NR^{1c}R^2)-$ ,  $-CR^2(OR^2)-$ ,  $-CR^2(SR^2)-$ ,  $-C(O)CR^2R^{2a}-$ ,  $-CR^2R^{2a}C(O)-$ ,  $-S-$ ,  $-S(O)-$ ,  $-S(O)_2-$ ,  $-SCR^2R^{2a}-$ ,  $-S(O)CR^2R^{2a}-$ ,  $-S(O)_2CR^2R^{2a}-$ ,  $-CR^2R^{2a}S-$ ,  $-CR^2R^{2a}S(O)-$ ,  $-CR^2R^{2a}S(O)_2-$ ,  $-S(O)_2NR^2-$ ,  $-NR^2S(O)_2-$ ,  $-NR^2S(O)_2CR^2R^{2a}-$ ,  $-CR^2R^{2a}S(O)_2NR^2-$ ,  $-NR^2S(O)_2NR^2-$ ,  $-C(O)NR^2-$ ,  $-NR^2C(O)-$ ,  $-C(O)NR^2CR^2R^{2a}-$ ,  $-NR^2C(O)CR^2R^{2a}-$ ,  $-CR^2R^{2a}C(O)NR^2-$ ,  $-CR^2R^{2a}NR^2C(O)-$ ,  $-NR^2C(O)O-$ ,  $-OC(O)NR^2-$ ,

$-\text{NR}^2\text{C}(\text{O})\text{NR}^2-$ ,  $-\text{NR}^2-$ ,  $-\text{NR}^2\text{CR}^2\text{R}^{2a}-$ ,  $-\text{CR}^2\text{R}^{2a}\text{NR}^2-$ ,  $\text{O}$ ,  
 $-\text{CR}^2\text{R}^{2a}\text{O}-$ , and  $-\text{OCR}^2\text{R}^{2a}-$ ;

Y is selected from:

- 5         $\text{C}_{3-10}$  carbocyclic residue substituted with 0-2  $\text{R}^{4a}$ , and  
       5-12 membered heterocyclic system comprising carbon  
 atoms and from 1-4 heteroatoms selected from the group  
 consisting of N, O, and S substituted with 0-2  $\text{R}^{4a}$ ;
- 10     $\text{R}^4$ , at each occurrence, is selected from H, =O,  $(\text{CH}_2)_r\text{OR}^2$ ,  
        $(\text{CH}_2)_r\text{F}$ ,  $(\text{CH}_2)_r\text{Cl}$ ,  $(\text{CH}_2)_r\text{Br}$ ,  $(\text{CH}_2)_r\text{I}$ ,  $\text{C}_{1-4}$  alkyl,  
        $(\text{CH}_2)_r\text{CN}$ ,  $(\text{CH}_2)_r\text{NO}_2$ ,  $(\text{CH}_2)_r\text{NR}^2\text{R}^{2a}$ ,  $\text{C}(\text{O})\text{R}^{2c}$ ,  $\text{NR}^2\text{C}(\text{O})\text{R}^{2b}$ ,  
        $\text{C}(\text{O})\text{NR}^2\text{R}^{2a}$ ,  $\text{NR}^2\text{C}(\text{O})\text{NR}^2\text{R}^{2a}$ ,  $\text{C}(=\text{NR}^2)\text{NR}^2\text{R}^{2a}$ ,  
        $\text{C}(=\text{NS}(\text{O})_2\text{R}^5)\text{NR}^2\text{R}^{2a}$ ,  $\text{NHC}(=\text{NR}^2)\text{NR}^2\text{R}^{2a}$ ,  $\text{C}(\text{O})\text{NHC}(=\text{NR}^2)\text{NR}^2\text{R}^{2a}$ ,  
 15     $\text{SO}_2\text{NR}^2\text{R}^{2a}$ ,  $\text{NR}^2\text{SO}_2\text{NR}^2\text{R}^{2a}$ ,  $\text{NR}^2\text{SO}_2-\text{C}_{1-4}$  alkyl,  $\text{NR}^2\text{SO}_2\text{R}^5$ ,  
        $\text{S}(\text{O})_p\text{R}^5$ ,  $(\text{CF}_2)_r\text{CF}_3$ ,  $(\text{CH}_2)_r-\text{CF}_3$ ,  $\text{NCH}_2\text{R}^{1c}$ ,  $\text{OCH}_2\text{R}^{1c}$ ,  $\text{SCH}_2\text{R}^{1c}$ ,  
        $\text{N}(\text{CH}_2)_2(\text{CH}_2)_t\text{R}^{1b}$ ,  $\text{O}(\text{CH}_2)_2(\text{CH}_2)_t\text{R}^{1b}$ ,  $\text{S}(\text{CH}_2)_2(\text{CH}_2)_t\text{R}^{1b}$ , 5-6  
       membered carbocycle substituted with 0-1  $\text{R}^5$ , and 5-6  
       membered heterocycle consisting of: carbon atoms and  
 20    1-4 heteroatoms selected from the group consisting of  
       N, O, and  $\text{S}(\text{O})_p$  substituted with 0-1  $\text{R}^5$ ;
- $\text{R}^{4a}$ , at each occurrence, is selected from H, =O,  $(\text{CH}_2)_r\text{OR}^2$ ,  
        $(\text{CF}_2)_r\text{CF}_3$ ,  $(\text{CH}_2)_r-\text{CF}_3$ ,  $(\text{CH}_2)_r-\text{F}$ ,  $(\text{CH}_2)_r-\text{Br}$ ,  $(\text{CH}_2)_r-\text{Cl}$ ,  
 25     $\text{C}_{1-4}$  alkyl,  $(\text{CH}_2)_r\text{CN}$ ,  $(\text{CH}_2)_r\text{NO}_2$ ,  $(\text{CH}_2)_r\text{NR}^2\text{R}^{2a}$ ,  
        $(\text{CH}_2)_r\text{C}(\text{O})\text{R}^{2c}$ ,  $\text{NR}^2\text{C}(\text{O})\text{R}^{2b}$ ,  $\text{C}(\text{O})\text{NR}^2\text{R}^{2a}$ ,  $(\text{CH}_2)_r\text{N}=\text{CHOR}^3$ ,  
        $\text{C}(\text{O})\text{NH}(\text{CH}_2)_2\text{NR}^2\text{R}^{2a}$ ,  $\text{NR}^2\text{C}(\text{O})\text{NR}^2\text{R}^{2a}$ ,  $\text{C}(=\text{NR}^2)\text{NR}^2\text{R}^{2a}$ ,  
        $\text{NHC}(=\text{NR}^2)\text{NR}^2\text{R}^{2a}$ ,  $\text{SO}_2\text{NR}^2\text{R}^{2a}$ ,  $\text{NR}^2\text{SO}_2\text{NR}^2\text{R}^{2a}$ ,  $\text{NR}^2\text{SO}_2-\text{C}_{1-4}$   
       alkyl,  $\text{NR}^2\text{SO}_2\text{R}^5$ ,  $\text{C}(\text{O})\text{NHSO}_2-\text{C}_{1-4}$  alkyl,  $\text{S}(\text{O})_p\text{R}^5$ , 5-6  
 30    membered carbocycle substituted with 0-1  $\text{R}^5$ , and 5-6  
       membered heterocycle consisting of: carbon atoms and  
       1-4 heteroatoms selected from the group consisting of  
       N, O, and  $\text{S}(\text{O})_p$  substituted with 0-1  $\text{R}^5$ ;

- $R^{4b}$ , at each occurrence, is selected from H, =O,  $(CH_2)_rOR^3$ ,  
 $(CH_2)_r-F$ ,  $(CH_2)_r-Cl$ ,  $(CH_2)_r-Br$ ,  $(CH_2)_r-I$ ,  $C_{1-4}$  alkyl,  
 $(CH_2)_r-CN$ ,  $(CH_2)_r-NO_2$ ,  $(CH_2)_rNR^3R^{3a}$ ,  $(CH_2)_rC(O)R^3$ ,  
5  $(CH_2)_rC(O)OR^{3c}$ ,  $NR^3C(O)R^{3a}$ ,  $C(O)NR^3R^{3a}$ ,  $NR^3C(O)NR^3R^{3a}$ ,  
 $C(=NR^3)NR^3R^{3a}$ ,  $NR^3C(=NR^3)NR^3R^{3a}$ ,  $SO_2NR^3R^{3a}$ ,  $NR^3SO_2NR^3R^{3a}$ ,  
 $NR^3SO_2-C_{1-4}$  alkyl,  $NR^3SO_2CF_3$ ,  $NR^3SO_2$ -phenyl,  $S(O)_pCF_3$ ,  
 $S(O)_p-C_{1-4}$  alkyl,  $S(O)_p$ -phenyl,  $(CH_2)_rCF_3$ , and  $(CF_2)_rCF_3$ ;
- 10  $R^5$ , at each occurrence, is selected from H,  $C_{1-6}$  alkyl, =O,  
 $(CH_2)_rOR^3$ , F, Cl, Br, I, -CN,  $NO_2$ ,  $(CH_2)_rNR^3R^{3a}$ ,  
 $(CH_2)_rC(O)R^3$ ,  $(CH_2)_rC(O)OR^{3c}$ ,  $NR^3C(O)R^{3a}$ ,  $C(O)NR^3R^{3a}$ ,  
 $NR^3C(O)NR^3R^{3a}$ ,  $CH(=NOR^{3d})$ ,  $C(=NR^3)NR^3R^{3a}$ ,  
 $NR^3C(=NR^3)NR^3R^{3a}$ ,  $SO_2NR^3R^{3a}$ ,  $NR^3SO_2NR^3R^{3a}$ ,  $NR^3SO_2-C_{1-4}$   
15 alkyl,  $NR^3SO_2CF_3$ ,  $NR^3SO_2$ -phenyl,  $S(O)_pCF_3$ ,  $S(O)_p-C_{1-4}$   
alkyl,  $S(O)_p$ -phenyl,  $(CF_2)_rCF_3$ , phenyl substituted with  
0-2  $R^6$ , naphthyl substituted with 0-2  $R^6$ , and benzyl  
substituted with 0-2  $R^6$ ;
- 20  $R^6$ , at each occurrence, is selected from H, OH,  $(CH_2)_rOR^2$ ,  
halo,  $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $(CH_2)_rNR^2R^{2a}$ ,  $(CH_2)_rC(O)R^{2b}$ ,  
 $NR^2C(O)R^{2b}$ ,  $NR^2C(O)NR^2R^{2a}$ ,  $C(=NH)NH_2$ ,  $NHC(=NH)NH_2$ ,  
 $SO_2NR^2R^{2a}$ ,  $NR^2SO_2NR^2R^{2a}$ , and  $NR^2SO_2C_{1-4}$  alkyl;
- 25  $R^7$ , at each occurrence, is selected from H, OH,  $C_{1-4}$   
alkoxycarbonyl,  $C_{6-10}$  aryloxy,  $C_{6-10}$  aryloxycarbonyl,  
 $C_{6-10}$  arylmethylcarbonyl,  $C_{1-4}$  alkylcarbonyloxy  $C_{1-4}$   
alkoxycarbonyl,  $C_{6-10}$  arylcarbonyloxy  $C_{1-4}$   
alkoxycarbonyl,  $C_{1-6}$  alkylaminocarbonyl,  
30 phenylaminocarbonyl, and phenyl  $C_{1-4}$  alkoxycarbonyl;

R<sup>8</sup>, at each occurrence, is selected from H, C<sub>1-6</sub> alkyl, and (CH<sub>2</sub>)<sub>n</sub>-phenyl;

alternatively, R<sup>7</sup> and R<sup>8</sup>, when attached to the same nitrogen,  
 5 combine to form a 5-6 membered heterocyclic ring consisting of carbon atoms and 0-2 additional heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>;

10 R<sup>9</sup>, at each occurrence, is selected from H, C<sub>1-6</sub> alkyl, and (CH<sub>2</sub>)<sub>n</sub>-phenyl;

n, at each occurrence, is selected from 0, 1, 2, and 3;

15 m, at each occurrence, is selected from 0, 1, and 2;

p, at each occurrence, is selected from 0, 1, and 2;

r, at each occurrence, is selected from 0, 1, 2, and 3;

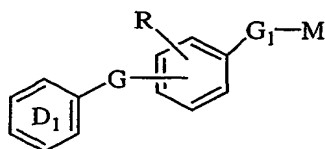
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s, at each occurrence, is selected from 0, 1, and 2; and,

t, at each occurrence, is selected from 0, 1, 2, and 3.

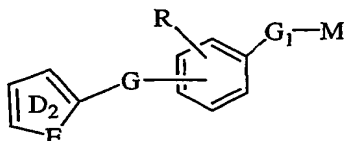
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2. A compound according to Claim 1, wherein the compound is of formula Ia<sub>1</sub>-Ic<sub>1</sub>, wherein:

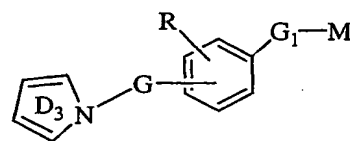


30

Ia<sub>1</sub>



Ib<sub>1</sub>



Ic<sub>1</sub>

ring D<sub>2</sub> is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-R<sup>c</sup> and ring D<sub>2</sub> is substituted with 1 R<sup>a</sup> and 0-1 R<sup>b</sup>;

5

ring D<sub>3</sub> is a 5-membered heteroaromatic ring system comprising carbon atoms and from 0-3 additional N atoms and ring D<sub>3</sub> is substituted with 1 R<sup>a</sup> and 0-1 R<sup>b</sup>;

10 R is selected from H, Cl, F, Br, I, OH, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

15 R<sup>a</sup> is selected from H, OH, SH, C<sub>1-3</sub> alkoxy, C<sub>1-3</sub> thioalkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

20 R<sup>b</sup> is selected from H, C<sub>1-4</sub> alkyl, Cl, F, Br, I, OH, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

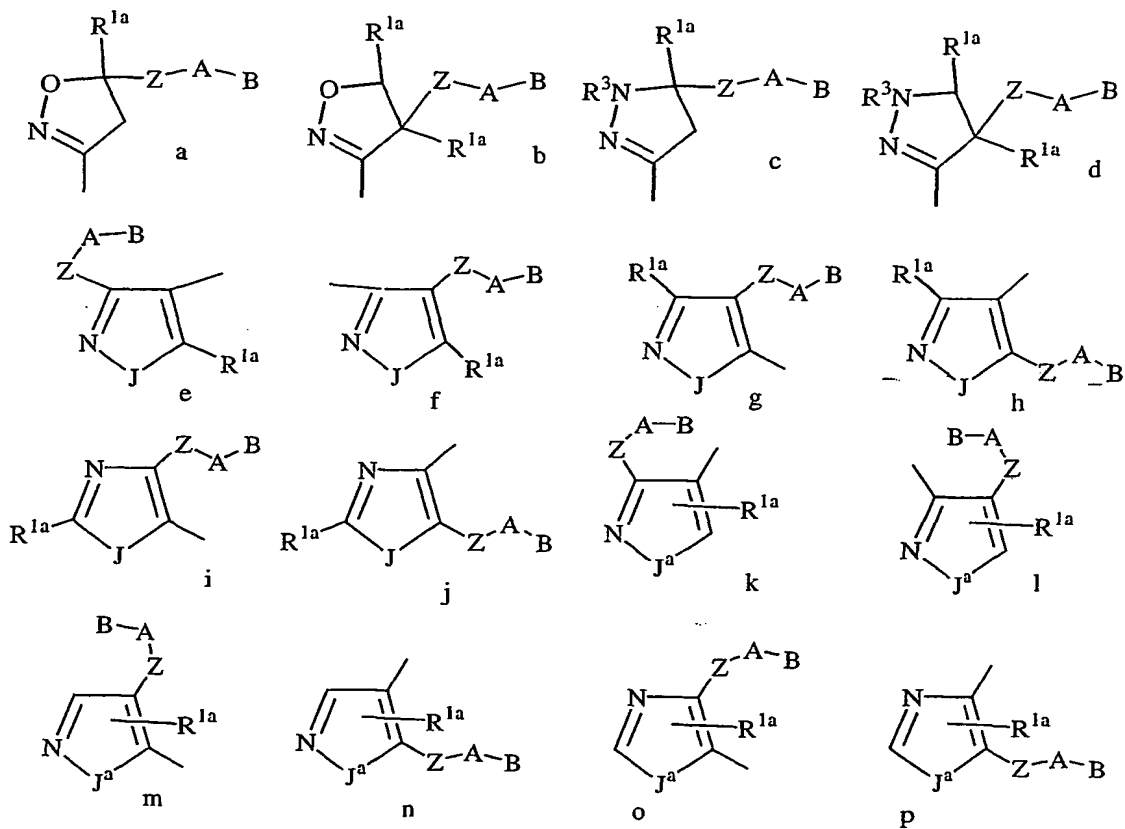
25 R<sup>c</sup> is selected from H, C<sub>1-4</sub> alkyl, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

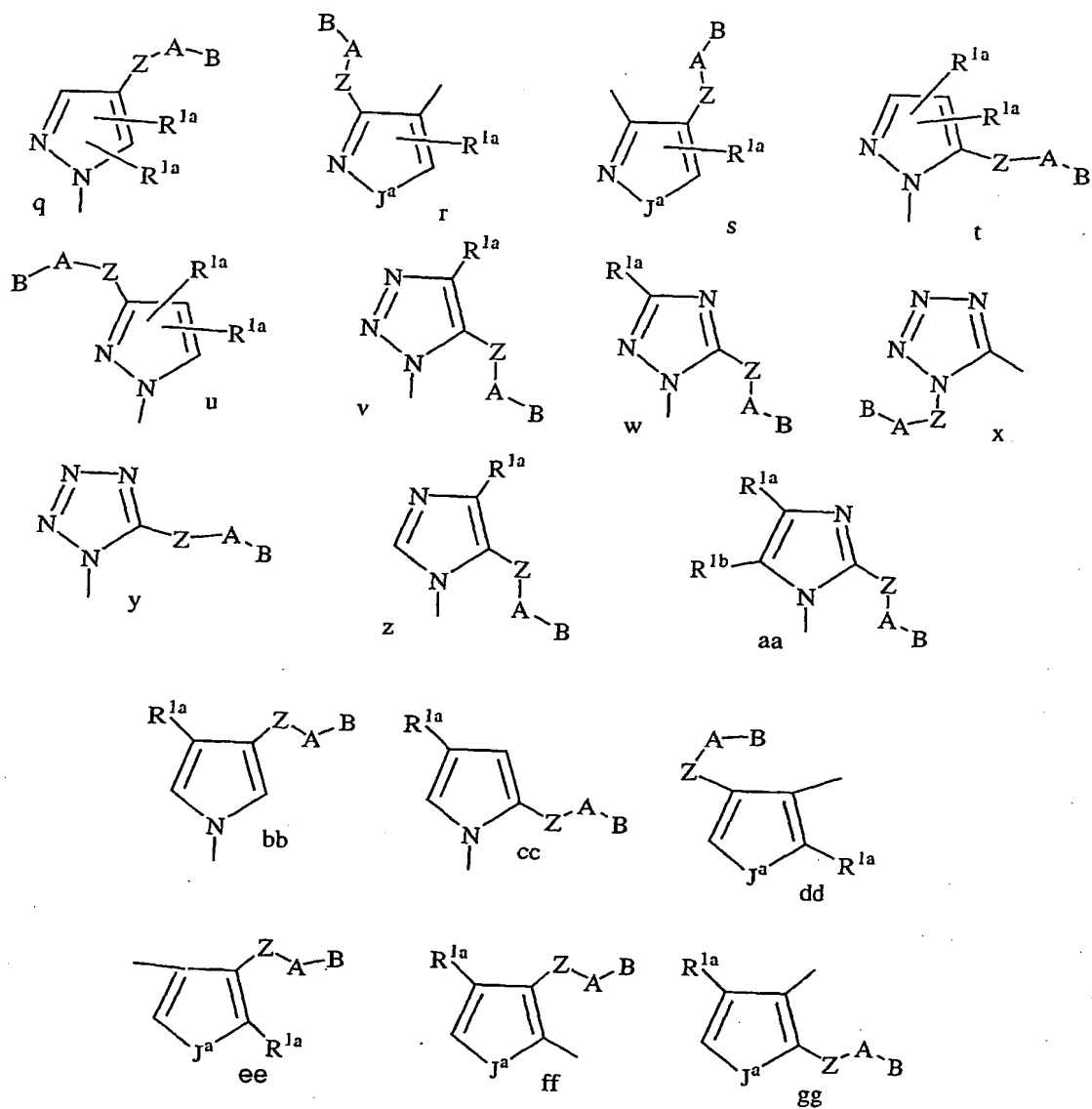
30 G<sub>1</sub> is absent or is selected from CH<sub>2</sub>, C(O), O, NR<sup>3</sup>, S(O)<sub>p</sub>, CH<sub>2</sub>CH<sub>2</sub>, C(O)CH<sub>2</sub>, CH<sub>2</sub>C(O), OCH<sub>2</sub>, CH<sub>2</sub>O, NR<sup>3</sup>CH<sub>2</sub>, CH<sub>2</sub>NR<sup>3</sup>, S(O)<sub>p</sub>CH<sub>2</sub>, CH<sub>2</sub>S(O)<sub>p</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>, C(O)CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>C(O)CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>C(O), OCH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>OCH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>O, NR<sup>3</sup>CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>NR<sup>3</sup>CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NR<sup>3</sup>, S(O)<sub>p</sub>CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>S(O)<sub>p</sub>CH<sub>2</sub>, and CH<sub>2</sub>CH<sub>2</sub>S(O)<sub>p</sub>, and

provided that G<sub>1</sub>-M form other than a N-N, O-N, or S-N bond;

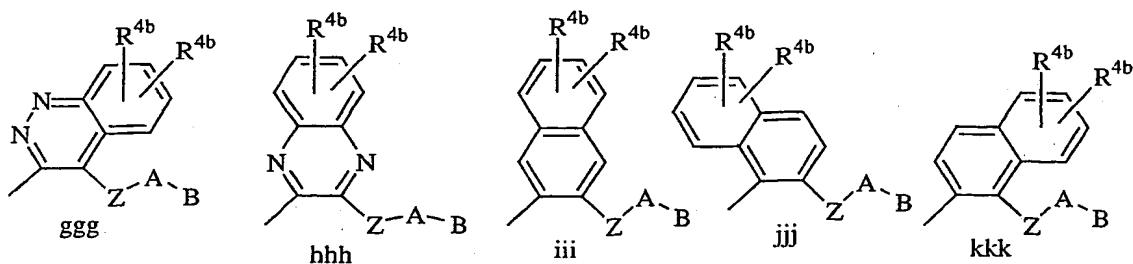
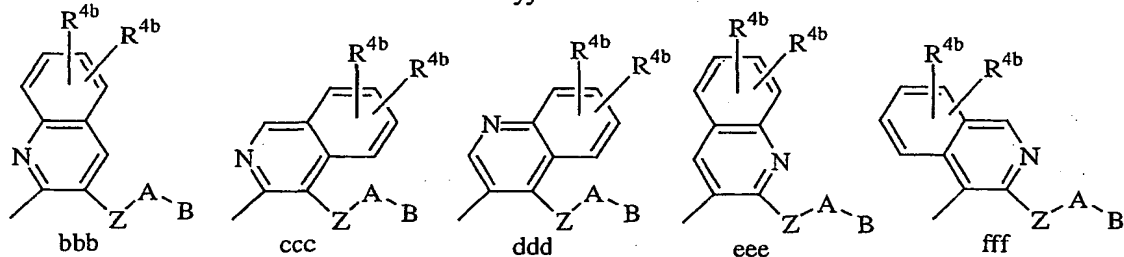
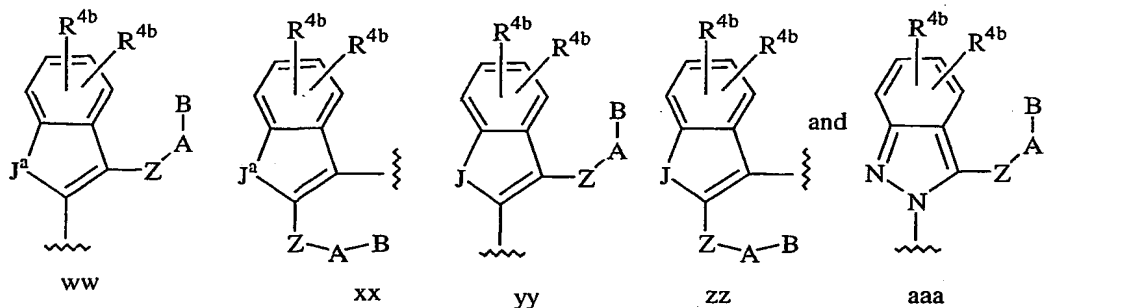
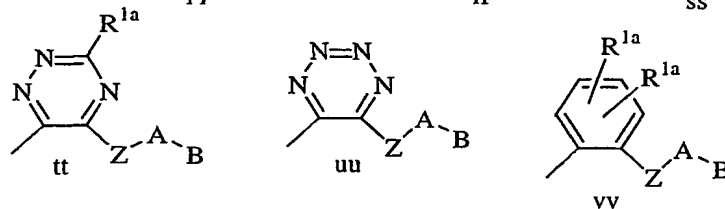
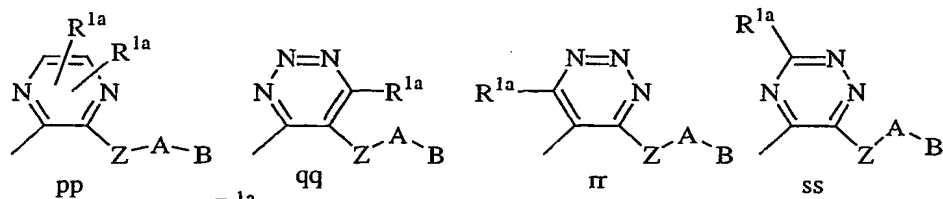
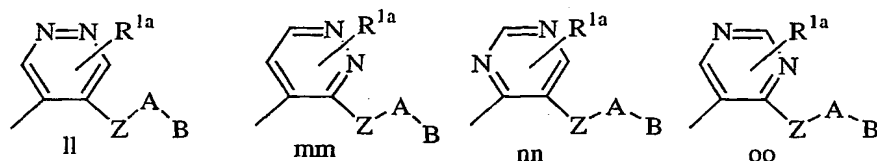
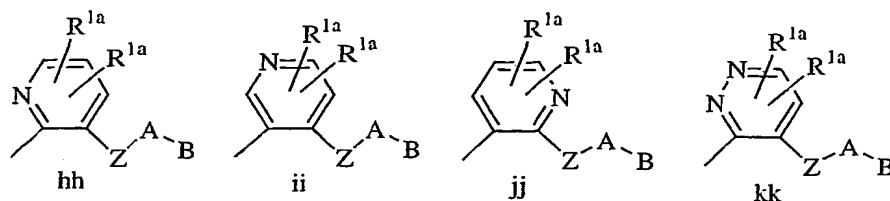
M is selected from the group:

5









J is O or S;

J<sup>a</sup> is NH or NR<sup>1a</sup>;

5

G<sub>1</sub> is absent or is selected from (CR<sup>3</sup>R<sup>3a</sup>)<sub>1-3</sub>,

(CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>C(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>O(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,

(CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>C(O)NR<sup>3</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,

(CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3</sup>C(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,

10 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(O)<sub>2</sub>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,

(CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(O)NR<sup>3</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, and (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(O)<sub>2</sub>NR<sup>3</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,

wherein u + w total 0, 1, or 2, provided that G<sub>1</sub> does not form a N-N, N-O, N-S, NCH<sub>2</sub>N, NCH<sub>2</sub>O, or NCH<sub>2</sub>S bond with either group to which it is attached;

15

A is selected from one of the following carbocyclic and heterocyclic systems which are substituted with 0-2 R<sup>4</sup>;

phenyl, piperidinyl, piperazinyl, pyridyl,

pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl,

20 pyrrolidinyl, oxazolyl, isoxazolyl, thiazolyl,

isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl,

thiadiazolyl, triazolyl, 1,2,3-oxadiazolyl,

1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl,

1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl,

25 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl,

1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl,

1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl,

benzothiofuranyl, indolyl, benzimidazolyl,

benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl,

30 benzisothiazolyl, and isoindazolyl;

X is selected from -(CR<sup>2</sup>R<sup>2a</sup>)<sub>1-4</sub>-, -C(O)-, -C(=NR<sup>1c</sup>)-,

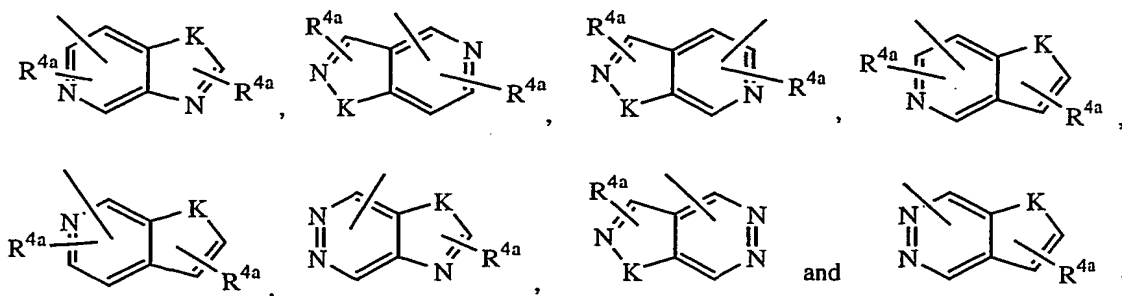
-CR<sup>2</sup>(NR<sup>1c</sup>CR<sup>2</sup>)-, -C(O)CR<sup>2</sup>R<sup>2a</sup>-, -CR<sup>2</sup>R<sup>2a</sup>C(O)-, -C(O)NR<sup>2</sup>-,

-NR<sup>2</sup>C(O)-, -C(O)NR<sup>2</sup>CR<sup>2</sup>R<sup>2a</sup>-, -NR<sup>2</sup>C(O)CR<sup>2</sup>R<sup>2a</sup>-;

$-\text{CR}^2\text{R}^{2a}\text{C}(\text{O})\text{NR}^2-$ ,  $-\text{CR}^2\text{R}^{2a}\text{NR}^2\text{C}(\text{O})-$ ,  $-\text{NR}^2\text{C}(\text{O})\text{NR}^2-$ ,  $-\text{NR}^2-$ ,  
 $-\text{NR}^2\text{CR}^2\text{R}^{2a}-$ ,  $-\text{CR}^2\text{R}^{2a}\text{NR}^2-$ ,  $\text{O}$ ,  $-\text{CR}^2\text{R}^{2a}\text{O}-$ , and  $-\text{OCR}^2\text{R}^{2a}-$ ;

Y is selected from one of the following carbocyclic and  
 5 heterocyclic systems that are substituted with 0-2  $\text{R}^{4a}$ ;  
 cyclopropyl, cyclopentyl, cyclohexyl, phenyl,  
 piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl,  
 morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl,  
 oxazolyl, isoxazolyl, isoxazolinyl, thiazolyl,  
 10 isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl,  
 thiadiazolyl, triazolyl, 1,2,3-oxadiazolyl,  
 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl,  
 1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl,  
 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl,  
 15 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl,  
 1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl,  
 benzothiofuranyl, indolyl, benzimidazolyl,  
 benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl,  
 benzisothiazolyl, and isoindazolyl;

alternatively, Y is selected from the following bicyclic  
 heteroaryl ring systems:



25 K is selected from O, S, NH, and N;

Z is selected from a bond,  $\text{CH}_2\text{O}$ ,  $\text{OCH}_2$ , NH,  $\text{CH}_2\text{NH}$ ,  $\text{NHCH}_2$ ,  
 $\text{CH}_2\text{C}(\text{O})$ ,  $\text{C}(\text{O})\text{CH}_2$ ,  $\text{C}(\text{O})\text{NH}$ ,  $\text{NHC}(\text{O})$ ,  $\text{CH}_2\text{S}(\text{O})_2$ ,  $\text{S}(\text{O})_2(\text{CH}_2)$ ,  
 $\text{SO}_2\text{NH}$ , and  $\text{NHSO}_2$ , provided that Z does not form a N-N,

N-O, N-S, NCH<sub>2</sub>N, NCH<sub>2</sub>O, or NCH<sub>2</sub>S bond with either group to which it is attached;

R<sup>4</sup>, at each occurrence, is selected from H, =O, (CH<sub>2</sub>)<sub>r</sub>OR<sup>2</sup>, F, Cl, Br, I, C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, (CH<sub>2</sub>)<sub>r</sub>NR<sup>2</sup>R<sup>2a</sup>, C(O)R<sup>2c</sup>, NR<sup>2</sup>C(O)R<sup>2b</sup>, C(O)NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>C(O)NR<sup>2</sup>R<sup>2a</sup>, C(=NR<sup>2</sup>)NR<sup>2</sup>R<sup>2a</sup>, SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>SO<sub>2</sub>-C<sub>1-4</sub> alkyl, NR<sup>2</sup>SO<sub>2</sub>R<sup>5</sup>, S(O)<sub>p</sub>R<sup>5</sup>, CF<sub>3</sub>, NCH<sub>2</sub>R<sup>1c</sup>, OCH<sub>2</sub>R<sup>1c</sup>, SCH<sub>2</sub>R<sup>1c</sup>, N(CH<sub>2</sub>)<sub>2</sub>(CH<sub>2</sub>)<sub>t</sub>R<sup>1b</sup>, O(CH<sub>2</sub>)<sub>2</sub>(CH<sub>2</sub>)<sub>t</sub>R<sup>1b</sup>, S(CH<sub>2</sub>)<sub>2</sub>(CH<sub>2</sub>)<sub>t</sub>R<sup>1b</sup>, 5-6 membered carbocycle substituted with 0-1 R<sup>5</sup>, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub> substituted with 0-1 R<sup>5</sup>; and,

R<sup>4a</sup>, at each occurrence, is selected from H, =O, (CH<sub>2</sub>)<sub>r</sub>OR<sup>2</sup>, CF<sub>3</sub>, F, Br, Cl, C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, (CH<sub>2</sub>)<sub>r</sub>NR<sup>2</sup>R<sup>2a</sup>, (CH<sub>2</sub>)<sub>r</sub>C(O)R<sup>2c</sup>, NR<sup>2</sup>C(O)R<sup>2b</sup>, C(O)NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>C(O)NR<sup>2</sup>R<sup>2a</sup>, C(=NR<sup>2</sup>)NR<sup>2</sup>R<sup>2a</sup>, NHC(=NR<sup>2</sup>)NR<sup>2</sup>R<sup>2a</sup>, SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>SO<sub>2</sub>-C<sub>1-4</sub> alkyl, NR<sup>2</sup>SO<sub>2</sub>R<sup>5</sup>, C(O)NHSO<sub>2</sub>-C<sub>1-4</sub> alkyl, S(O)<sub>p</sub>R<sup>5</sup>, 5-6 membered carbocycle substituted with 0-1 R<sup>5</sup>, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub> substituted with 0-1 R<sup>5</sup>.

3. A compound according to Claim 2, wherein the compound is of formula Ib<sub>1</sub> or Ic<sub>1</sub>, wherein:

ring D<sub>2</sub> is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-R<sup>c</sup> and ring D<sub>2</sub> is substituted with 1 R<sup>a</sup> and 0-1 R<sup>b</sup>;

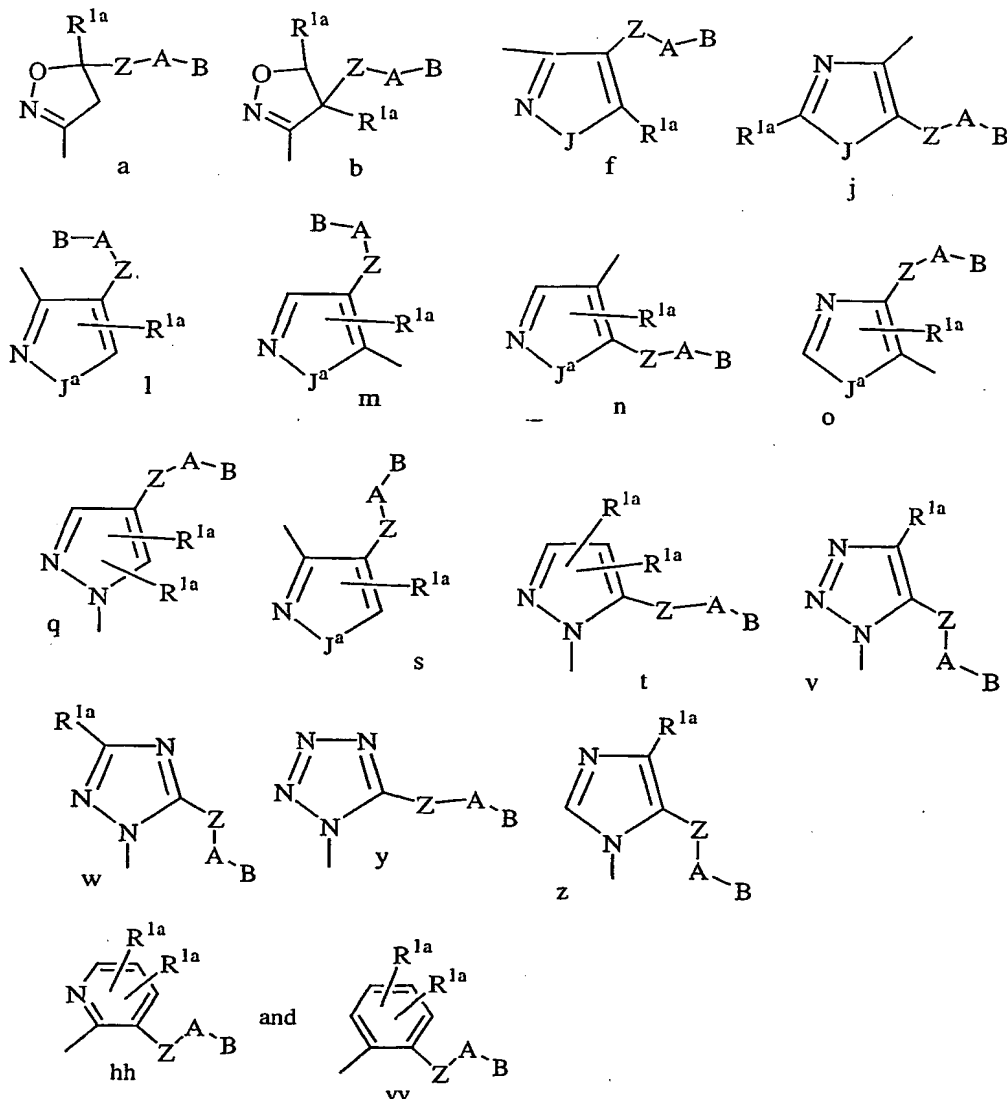
R is selected from H, Cl, F, Br, I, OH, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

5 R<sup>a</sup> is selected from H, OH, SH, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

10 R<sup>b</sup> is selected from H, C<sub>1-4</sub> alkyl, Cl, F, Br, I, OH, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

15 R<sup>c</sup> is selected from H, C<sub>1-4</sub> alkyl, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

M is selected from the group:



Y is selected from one of the following carbocyclic and heterocyclic systems which are substituted with 0-2  $R^{4a}$ ;

- 5           phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazole, thiadiazole, triazole, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadiazole, 1,2,3-triazole, 1,2,4-triazole, 1,2,5-triazole, 1,3,4-triazole, benzofuran,
- 10

benzothiofuran, indole, benzimidazole, benzimidazolone, benzoxazole, benzthiazole, indazole, benzisoxazole, benzisothiazole, and isoindazole;

5 Z is selected from a bond,  $\text{CH}_2\text{O}$ ,  $\text{OCH}_2$ ,  $\text{NH}$ ,  $\text{CH}_2\text{NH}$ ,  $\text{NHCH}_2$ ,  $\text{CH}_2\text{C}(\text{O})$ ,  $\text{C}(\text{O})\text{CH}_2$ ,  $\text{C}(\text{O})\text{NH}$ ,  $\text{NHC}(\text{O})$ ,  $\text{CH}_2\text{S}(\text{O})_2$ ,  $\text{S}(\text{O})_2(\text{CH}_2)$ ,  $\text{SO}_2\text{NH}$ , and  $\text{NHSO}_2$ , provided that Z does not form a N-N, N-O, N-S,  $\text{NCH}_2\text{N}$ ,  $\text{NCH}_2\text{O}$ , or  $\text{NCH}_2\text{S}$  bond with either group to which it is attached;

10

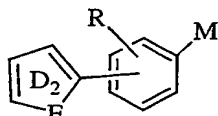
$\text{R}^4$ , at each occurrence, is selected from H,  $=\text{O}$ ,  $(\text{CH}_2)_r\text{OR}^2$ , F, Cl, Br, I,  $\text{C}_{1-4}$  alkyl, CN,  $\text{NO}_2$ ,  $(\text{CH}_2)_r\text{NR}^2\text{R}^{2a}$ ,  $\text{C}(\text{O})\text{R}^{2c}$ ,  $\text{NR}^2\text{C}(\text{O})\text{R}^{2b}$ ,  $\text{C}(\text{O})\text{NR}^2\text{R}^{2a}$ ,  $\text{NR}^2\text{C}(\text{O})\text{NR}^2\text{R}^{2a}$ ,  $\text{C}(=\text{NR}^2)\text{NR}^2\text{R}^{2a}$ ,  $\text{SO}_2\text{NR}^2\text{R}^{2a}$ ,  $\text{NR}^2\text{SO}_2\text{NR}^2\text{R}^{2a}$ ,  $\text{NR}^2\text{SO}_2\text{-C}_{1-4}$  alkyl,  $\text{NR}^2\text{SO}_2\text{R}^5$ ,  
15  $\text{S}(\text{O})_p\text{R}^5$ ,  $\text{CF}_3$ , 5-6 membered carbocycle substituted with 0-1  $\text{R}^5$ , and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $\text{S}(\text{O})_p$  substituted with 0-1  $\text{R}^5$ ; and,

20

$\text{R}^{4a}$ , at each occurrence, is selected from H,  $=\text{O}$ ,  $(\text{CH}_2)_r\text{OR}^2$ ,  $\text{CF}_3$ , F, Br, Cl,  $\text{C}_{1-4}$  alkyl, CN,  $\text{NO}_2$ ,  $(\text{CH}_2)_r\text{NR}^2\text{R}^{2a}$ ,  $(\text{CH}_2)_r\text{C}(\text{O})\text{R}^{2c}$ ,  $\text{NR}^2\text{C}(\text{O})\text{R}^{2b}$ ,  $\text{C}(\text{O})\text{NR}^2\text{R}^{2a}$ ,  $\text{NR}^2\text{C}(\text{O})\text{NR}^2\text{R}^{2a}$ ,  $\text{C}(=\text{NR}^2)\text{NR}^2\text{R}^{2a}$ ,  $\text{SO}_2\text{NR}^2\text{R}^{2a}$ ,  $\text{C}(\text{O})\text{NHSO}_2\text{-C}_{1-4}$  alkyl,  $\text{S}(\text{O})_p\text{R}^5$ ,  
25 5-6 membered carbocycle substituted with 0-1  $\text{R}^5$ , and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $\text{S}(\text{O})_p$  substituted with 0-1  $\text{R}^5$ .

30

4. A compound according to Claim 3, wherein the compound is of formula  $\text{Ib}_2$ :

Ib<sub>2</sub>

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

5

ring D<sub>2</sub> is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-R<sup>c</sup> and ring D<sub>2</sub> is substituted with 1 R<sup>a</sup> and 0-1 R<sup>b</sup>;

10

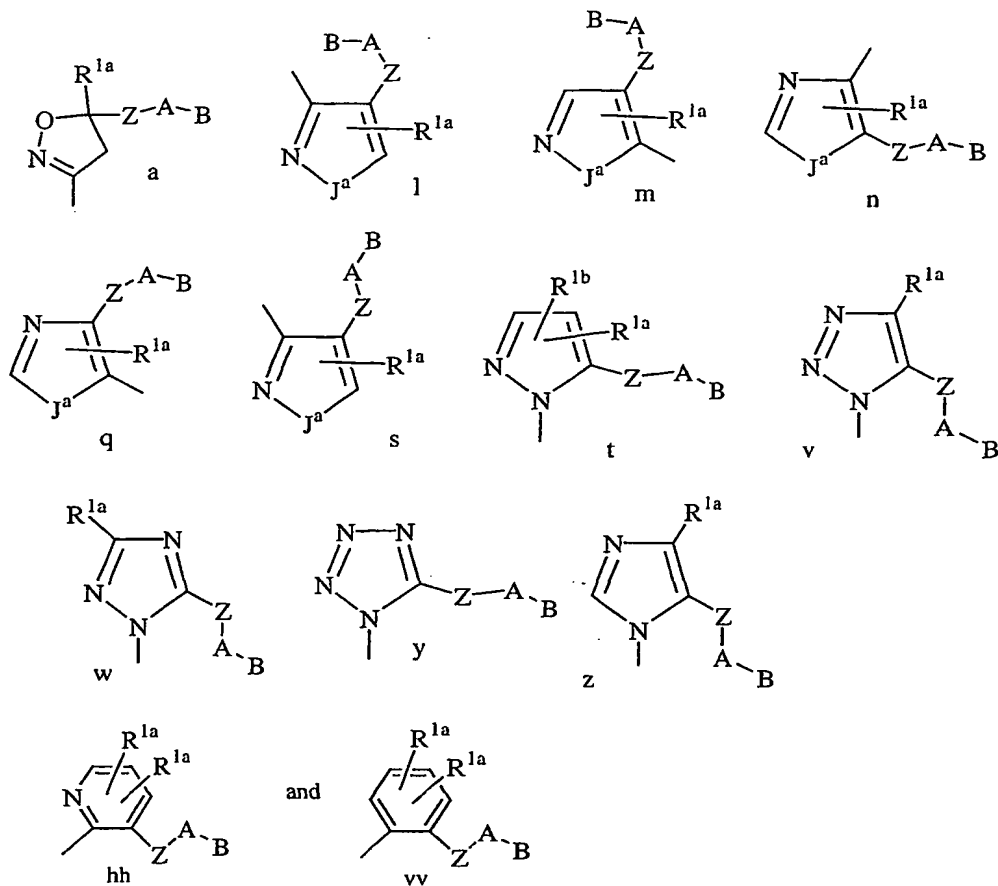
R is selected from H, Cl, F, Br, I, OH, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

15 R<sup>a</sup> is selected from H, OH, SH, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), and N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

R<sup>b</sup> is selected from H, C<sub>1-4</sub> alkyl, Cl, F, Br, I, OH, C<sub>1-3</sub> alkoxy, NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>,  
20 CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), and CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>;

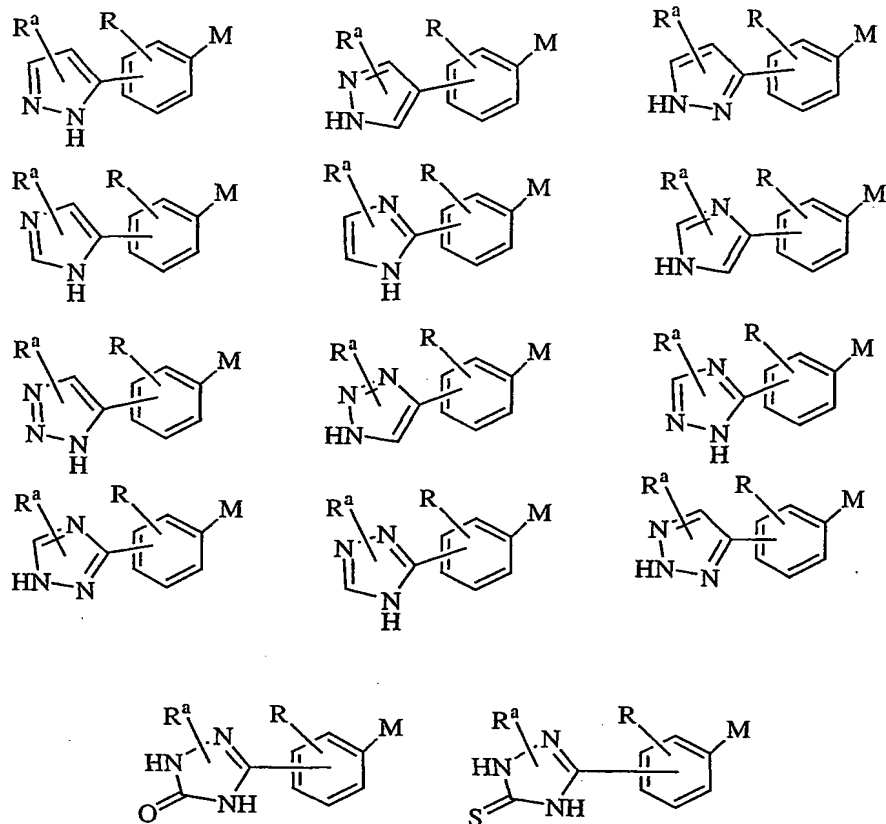
M is selected from the group:





G<sub>1</sub> is absent or is selected from CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>O, OCH<sub>2</sub>, NH, CH<sub>2</sub>NH, NHCH<sub>2</sub>, CH<sub>2</sub>C(O), C(O)CH<sub>2</sub>, C(O)NH, NHC(O), CH<sub>2</sub>S(O)<sub>2</sub>, S(O)<sub>2</sub>(CH<sub>2</sub>), SO<sub>2</sub>NH, and NHSO<sub>2</sub>, provided that G<sub>1</sub> does not form a N-N, N-O, N-S, NCH<sub>2</sub>N, NCH<sub>2</sub>O, or NCH<sub>2</sub>S bond with either group to which it is attached.

5. A compound according to Claim 4, wherein the compound is selected from one of the formulas:



5 or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

$G_1$  is absent;

10 A is selected from phenyl, piperidinyl, pyridyl, and pyrimidyl, and is substituted with 0-2  $R^4$ ; and,

B is selected from phenyl, pyrrolidino, N-pyrrolidino-carbonyl, morpholino, N-morpholino-carbonyl, 1,2,3-  
 15 triazolyl, imidazolyl, and benzimidazolyl, and is substituted with 0-1  $R^{4a}$ ;

$R^2$ , at each occurrence, is selected from H,  $CH_3$ ,  $CH_2CH_3$ , cyclopropylmethyl, cyclobutyl, and cyclopentyl;

20

R<sup>2a</sup>, at each occurrence, is selected from H, CH<sub>3</sub>, and CH<sub>2</sub>CH<sub>3</sub>;

alternatively, R<sup>2</sup> and R<sup>2a</sup>, together with the atom to which they are attached, combine to form pyrrolidine

5 substituted with 0-2 R<sup>4b</sup> or piperidine substituted with 0-2 R<sup>4b</sup>;

R<sup>4</sup>, at each occurrence, is selected from OH, OR<sup>2</sup>, (CH<sub>2</sub>)OR<sup>2</sup>, (CH<sub>2</sub>)<sub>2</sub>OR<sup>2</sup>, F, Br, Cl, I, C<sub>1-4</sub> alkyl, NR<sup>2</sup>R<sup>2a</sup>, (CH<sub>2</sub>)NR<sup>2</sup>R<sup>2a</sup>,  
10 (CH<sub>2</sub>)<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, CF<sub>3</sub>, and (CF<sub>2</sub>)CF<sub>3</sub>;

R<sup>4a</sup> is selected from C<sub>1-4</sub> alkyl, CF<sub>3</sub>, OR<sup>2</sup>, (CH<sub>2</sub>)OR<sup>2</sup>, (CH<sub>2</sub>)<sub>2</sub>OR<sup>2</sup>, NR<sup>2</sup>R<sup>2a</sup>, (CH<sub>2</sub>)NR<sup>2</sup>R<sup>2a</sup>, (CH<sub>2</sub>)<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, SR<sup>5</sup>, S(O)R<sup>5</sup>, S(O)<sub>2</sub>R<sup>5</sup>, SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, and 1-CF<sub>3</sub>-tetrazol-2-yl;

15

R<sup>4b</sup>, at each occurrence, is selected from H, CH<sub>3</sub>, and OH;

R<sup>5</sup>, at each occurrence, is selected from CF<sub>3</sub>, C<sub>1-6</sub> alkyl, phenyl, and benzyl; and,

20

r, at each occurrence, is selected from 0, 1, and 2.

6. A compound according to Claim 5, wherein:

25

A is selected from the group: phenyl, piperidinyl, 2-pyridyl, 3-pyridyl, 2-pyrimidyl, 2-Cl-phenyl, 3-Cl-phenyl, 2-F-phenyl, 3-F-phenyl, 2-methylphenyl, 2-aminophenyl, and 2-methoxyphenyl; and,

30

B is selected from the group: 2-(aminosulfonyl)phenyl, 2-(methylaminosulfonyl)phenyl, 1-pyrrolidinocarbonyl, 2-(methylsulfonyl)phenyl, 2-(N,N-dimethylaminomethyl)phenyl, 2-(N-

methylaninomethyl)phenyl, 2-(N-ethyl-N-methylaninomethyl)phenyl, 2-(N-pyrrolidinylmethyl)phenyl, 1-methyl-2-imidazolyl, 2-methyl-1-imidazolyl, 2-(dimethylaninomethyl)-1-imidazolyl, 2-(methylaninomethyl)-1-imidazolyl, 2-(N-(cyclopropylmethyl)aminomethyl)phenyl, 2-(N-(cyclobutyl)aminomethyl)phenyl, 2-(N-(cyclopentyl)aminomethyl)phenyl, 2-(N-(4-hydroxypiperidinyl)methyl)phenyl, and 2-(N-(3-hydroxypyrrolidinyl)methyl)phenyl.

7. A compound according to Claim 1, wherein the compound is selected from the group:

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-5-[(2'-N,N-dimethylaninomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-5-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N,N-dimethylaninomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-5-[(2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

5

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

10 1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

15 1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

20 1-[3-(2'-Amino-3',4'-thiadiazol-5'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

25 1-[3-(2'-Amino-3',4'-thiadiazol-5'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

30 1-[3-(2'-Amino-3',4'-thiadiazol-5'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

35 1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-5-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]pyrazole;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-5-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl]aminocarbonyl]pyrazole;

5

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

10 1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

15 1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

20 1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

25 1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-5-[(3-fluoro-2'-sulfonylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]pyrazole;

30 1-[3-(5-Amino-1,3,4-oxadiazol-2-yl)phenyl]-N-{2'-[(dimethylamino)methyl]-3-fluoro-1,1'-biphenyl-4-yl}-3-(trifluoromethyl)-1H-pyrazole-5-carboxamide;

35 1-[3-(5-Amino-1,3,4-oxadiazol-2-yl)phenyl]-N-(3-fluoro-2'-{[(3S)-3-hydroxy-1-pyrrolidinyl]methyl}-1,1'-biphenyl-

4-yl)-3-(trifluoromethyl)-1H-pyrazole-5-carboxamide;  
and,

1-[3-(5-Amino-1,3,4-oxadiazol-2-yl)phenyl]-N-(3-fluoro-2'-  
5        {[(3S)-3-hydroxy-1-pyrrolidinyl]methyl}-1,1'-biphenyl-  
4-yl)-5-(trifluoromethyl)-1H-pyrazole-3-carboxamide;

or a pharmaceutically acceptable salt thereof.

10

8. A pharmaceutical composition, comprising: a  
pharmaceutically acceptable carrier and a therapeutically  
effective amount of a compound of Claim 1, 2, 3, 4, 5, 6, or  
7 or a pharmaceutically acceptable salt form thereof.

15

9. A method for treating or preventing a thromboembolic  
disorder, comprising: administering to a patient in need  
thereof a therapeutically effective amount of a compound of  
20 Claim 1, 2, 3, 4, 5, 6, or 7 or a pharmaceutically  
acceptable salt form thereof.

10. A compound of Claim 1, 2, 3, 4, 5, 6, or 7 for use  
25 in therapy.

11. Use of a compound of Claim 1, 2, 3, 4, 5, 6, or 7  
for the manufacture of a medicament for the treatment of a  
30 thromboembolic disorder.

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 01/20112

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D403/10 C07D417/10 C07D403/14 C07D417/14 C07D401/10  
C07D413/10 C07D413/14 A61K31/41 A61K31/44 A61P7/02

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BEILSTEIN Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 28269 A (DUPONT MERCK) 2 July 1998 (1998-07-02) page 1, line 1 -page 3, line 33; claims; examples	1,8-11
X	US 6 020 357 A (PINTO ET. AL.) 1 February 2000 (2000-02-01) column 1, line 1 -column 2, line 65; claims; examples	1,8-11
P,X	WO 00 59902 A (DU PONT) 12 October 2000 (2000-10-12) page 78, line 1 - line 27; claims; examples	1,8-11
P,X	WO 00 53264 A (DU PONT) 14 September 2000 (2000-09-14) page 4, line 10 -page 5, line 25; claims	1,8-11
	-/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
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- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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- \*Z\* document member of the same patent family

Date of the actual completion of the international search

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Date of mailing of the international search report

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## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 01/20112

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 939 418 A (QUAN ET. AL.) 17 August 1999 (1999-08-17) claims; examples ---	1-11
A	DE 198 19 548 A (MERCK PATENT GMBH) 4 November 1999 (1999-11-04) page 2, line 44 - line 69; claims; examples -----	1-11

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/20112

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9828269	A	02-07-1998	AU 730224 B2	01-03-2001
			AU 5602098 A	17-07-1998
			CN 1246847 A	08-03-2000
			EE 9900316 A	15-02-2000
			EP 0946508 A1	06-10-1999
			HR 970698 A1	31-10-1998
			HU 0000735 A2	28-04-2001
			JP 2001509145 T	10-07-2001
			LT 99076 A ,B	25-02-2000
			LV 12430 A	20-02-2000
			LV 12430 B	20-07-2000
			NO 992633 A	20-08-1999
			PL 334250 A1	14-02-2000
			SI 20017 A	29-02-2000
			SK 86699 A3	07-11-2000
			WO 9828269 A1	02-07-1998
			US 6020357 A	01-02-2000
			BR 9714073 A	09-05-2000
US 6020357	A	01-02-2000	AU 730224 B2	01-03-2001
			AU 5602098 A	17-07-1998
			CN 1246847 A	08-03-2000
			EE 9900316 A	15-02-2000
			EP 0946508 A1	06-10-1999
			HR 970698 A1	31-10-1998
			HU 0000735 A2	28-04-2001
			JP 2001509145 T	10-07-2001
			LT 99076 A ,B	25-02-2000
			LV 12430 A	20-02-2000
			LV 12430 B	20-07-2000
			NO 992633 A	20-08-1999
			PL 334250 A1	14-02-2000
			SI 20017 A	29-02-2000
			SK 86699 A3	07-11-2000
			WO 9828269 A1	02-07-1998
			BR 9714073 A	09-05-2000
WO 0059902	A	12-10-2000	AU 4327600 A	23-10-2000
			WO 0059902 A2	12-10-2000
WO 0053264	A	14-09-2000	WO 0053264 A1	14-09-2000
US 5939418	A	17-08-1999	AU 1335897 A	17-07-1997
			CA 2240946 A1	03-07-1997
			EP 0874629 A1	04-11-1998
			HR 960597 A1	30-04-1998
			JP 2001502655 T	27-02-2001
			WO 9723212 A1	03-07-1997
DE 19819548	A	04-11-1999	DE 19819548 A1	04-11-1999
			AU 3815499 A	23-11-1999
			BR 9910021 A	26-12-2000
			CN 1299343 T	13-06-2001
			WO 9957096 A1	11-11-1999
			EP 1076643 A1	21-02-2001
			HU 0102220 A2	28-10-2001
			NO 20005435 A	27-10-2000
			PL 343598 A1	27-08-2001

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